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A SYMPOSIUM ON ELECTROLYTES[1]

INTRODUCTION TO THE SYMPOSIUM

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Received July 28, 1933

The past decade has witnessed advances in our knowledge of solutions and particularly of electrolytic solutions, which are second in importance only to the revolutionary innovations introduced fifty years ago by van't Hoff, Arrhenius, Ostwald, and Nernst. In view of the far reaching consequences of the important contributions of Debye and Hückel, it is eminently fitting that this symposium is being held on the tenth anniversary of the appearance of their fundamental papers.

During the past decade the problems of electrolytes have been subjected to a consistent and rational thermodynamic analysis, using methods which have proven to be well adapted for expressing the results of the more powerful tools of statistical mechanics. As a result the main features of the interaction problem have been solved sufficiently well for dilute aqueous solutions, so that today there are few who doubt the utility of considering strong electrolytes as practically completely dissociated in such solvents. The interpretation of the behavior of electrolytes in low dielectric solvents constitutes the pressing problem of the present. Here again statistical mechanics is the guiding light. The important paper of Fuoss and Kraus (1) presented at this symposium had already been accepted for publication elsewhere and unfortunately does not appear in the present list.

The prompt and cordial reception which the theory of Debye and Hückel received was due in no small measure to the fact that several investigators had just deduced on non-mathematical grounds the essential features of the theory which Debye and Hückel, working quite independently, presented in a single equation as a mathematical result of similar initial postulates. I refer to the discovery of the principle of ionic strength by Lewis and Randall in 1921 and to the principle of electric charge types enunciated by Brönsted as a result of the extensive experimental studies made in his laboratory. Reasoning from fundamental principles and guided by the data, Brönsted predicted in 1922 the form which the limiting law must assume and the universal character of the theoretical constant. It was the writer's good fortune to be engaged in the determination of the value of this constant, when the paper of Debye and Hückel appeared predicting the numerical value we were finding experimentally.

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[1] This symposium on electrolytes was held by the Division of Physical and Inorganic Chemistry at the eighty-fifth meeting of the American Chemical Society in Washington, D. C., in March, 1933.

[2] Chairman of the symposium.

The rare skill with which Brönsted has utilized these principles in unravelling the still more subtle problems of neutral salt catalysis and of acid and basic catalysis constitutes one of the most brilliant chemical achievements of the decade. These kinetic aspects have been treated in detail in recent symposia published in This Journal (2), so that the present symposium will be confined primarily to non-kinetic problems.

In the opening paper Scatchard (p. 7) reviews the subject from the historical point of view in a most engaging manner, and develops the Debye picture of the ionic atmosphere which is applied to reversible and non-reversible processes. His presentation of the chemical and physical views of association is timely and should be of aid in dissipating the fog of confusion with which some writers have enveloped the subject. In a later paper with Prentiss (p. 139) an objective evaluation of certain data is presented.

The precise measurement of transference number has long been recognized as a master key for interpreting the intricacies of conductance data, but in contrast to the latter the measurements remained notoriously difficult, inaccurate, and meager until MacInnes and his collaborators developed the moving boundary technique into a precision method. In their paper, MacInnes, Shedlowsky, and Longsworth (p. 29) report conductance data to 3×10^{-5} M with an accuracy of 0.02 per cent, along with transference data of comparable accuracy—a notable advance over Kohlrausch's classic achievements. The Arrhenius theory postulated a constant transference number, which was not always in agreement with the available data. It is highly significant that the variations in transference number which are obtained by the refined methods now available are in the direction and magnitude predicted by Onsager's form of the interionic attraction theory. By utilizing the results on strong electrolytes MacInnes and his collaborators have revised the dissociation constants of weak electrolytes, with the result that conductance data are now in perfect agreement with purely thermodynamic data.

Onsager's paper (p. 73), a searching critique of the statistical foundations of the Debye theory, merits a careful study by anyone who wishes to penetrate the subject. The first important result is equation 9 which states that the potential to be employed in the distribution law is the *potential of the average force.* The Guntelberg single ion charging process and the Debye form of the charging process are shown to be equally valid procedures.

The paradox to which the late Dr. T. H. Gronwall and the writer called attention some six years ago, namely, that the two procedures do not yield the same result when applied to the general solution of the Poisson-Boltzmann equation, is attributed by Onsager to an inconsistency in the fundamental equation. Halpern (3), working independently of Onsager, has reached the same conclusion.

Stated physically it appears that the average distribution of charge produced by a pair of ions i and j at a distance r is not always the precise sum of the charges induced by the two ions separately. From Halpern's studies it appears that this will occur whenever the individual ion diameters differ or the valences are not symmetrical. The assumption of spherical symmetry about one ion precludes the similar and simultaneous assumption for the other ion when in the presence of the first. In other words, the fields of individual ions cannot in general be exactly superimposed except for extremely dilute solutions where the limiting law is an adequate approximation.

It is indeed comforting to learn from Onsager that most of the error due to the neglect of fluctuation terms cancels out.

One of the criticisms which could be justly levelled against physical chemistry has been the great concern for aqueous chemistry to the unwarranted exclusion of the non-aqueous. Downes and the writer (p. 47) point out the inadequacy of the classical concepts of acids and bases for understanding their behavior in non-aqueous solvents. The complete absence of acid and basic properties makes the hydrocarbons a most interesting and important type of solvent for investigating the behavior of acid and bases. For this reason we have chosen benzene as a typical example of such an extreme type of solvent for the application of indicator and electrometric methods for the determination of acid strengths. Quantitative measurements, which recognize the influence of association, are reported for a series of sixteen acid–base systems and the results compared with those in aqueous solution.

Hammett (p. 61) treats the problem of the dissociation constants of bases which are too weak for measurement in water from a similar viewpoint. By using concentrated sulfuric acid as a typical acid solvent he demonstrates how the latent basic properties of oxygen-bearing compounds like ketones and aldehydes can be subjected to quantitative study.

The Kilpatricks (p. 131) have chosen acetonitrile as an example of a weakly basic solvent and by indicator methods have correlated the strengths of many acid–base systems in this solvent.

The salting-out effect is a phenomenon of wide application that has been studied for many years. It represents the interaction of ions upon neutral molecules. Gross (p. 91) surveys this broad field and proposes a theory of the antagonistic action of cations and anions as an explanation of "salting out" and "salting in."

Long familiarity with the subject makes Young (p. 103) particularly well qualified to discuss the errors which enter into the intricate calculation of the activity coefficients of concentrated solutions from freezing point data. It appears that the discrepancies between the E.M.F. and freezing point computations which still persist after Young's improved treatment are due primarily to inaccuracies in the original data.

Thermodynamics teaches that the relatively minute changes in volume and compressibility of the solvent which are produced by the addition of a solute are correlated with the changes in the thermal property of heat capacity. The interionic attraction theory predicts that these properties should involve the first and second derivatives of the dielectric constant with respect to volume, temperature, or pressure as the case may be. Unfortunately the numerical values of these derivatives are uncertain, owing to experimental inaccuracies, so that quantitative comparisons with theory are necessarily of doubtful significance. Nevertheless it appears that the experimental data on molal volumes, heat capacities, and compressibilities may often be represented by comparatively simple formulas involving only the square root of the concentration for considerable range. Gucker in his paper (p. 111) discusses these interesting results for this new yet difficult field of investigation.

The Division of Physical and Inorganic Chemistry of The American Chemical Society is much indebted to its Chairman of the year, Professor W. A. Noyes, Jr. for initiating this successful symposium and for his untiring efforts in its organization.

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(2) Chem. Rev. **5**, 231–338 (1928); **10**, 1–264 (1932).
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THE COMING OF AGE OF THE INTERIONIC ATTRACTION THEORY[1]

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Received May 11, 1933

In April, 1912, Milner (34) published his paper entitled "The Virial of a Mixture of Ions," and in May, 1923, Debye and Hückel (11) published their first paper, "Zur Theorie der Elektrolyte." So this meeting falls very close to the tenth and the twenty-first anniversaries of the two most important events in the theoretical study of interionic attraction. If the first publication of a quantitative relation may be considered as the birth of a theory, the interionic attraction theory comes of age next month. The present occasion is then a very fitting one to stop and consider just what this adolescent theory is, what it has already accomplished, what may be expected of it in the future, and what our attitude toward it is to be.

To judge any theory we must consider its predecessors and important contemporaries. In this case we need not go back very far into history, but we may start in 1885 with the two theories introduced in the first great papers of Arrhenius (2). The first, the theory of "ionic dissociation," states that the ions are not formed by the electrical field but exist in considerable quantities in electrolyte solutions in the absence of any external electrical force. This theory has been the basis of all subsequent studies in this field, and every new development has confirmed it. The second theory states that dissolved electrolytes are sharply divided into two parts without transition stages: the ions, which are entirely independent of each other and behave as ideal solutes;

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[1] Contribution No. 307 from the Research Laboratory of Physical Chemistry of the Massachusetts Institute of Technology.

and the undissociated molecules, in which two or more ions are so tightly held together that they behave as a single ideal solute molecule. This is generally known as the theory of "partial ionic dissociation." The theory is quite symmetrical, however, and we, who are no longer shocked at the idea of free ions, might equally well call it the theory of "partial association." Although it has not at all the standing of the first theory, it has been much more emphasized for the reason that it leads to important quantitative conclusions. Its successes have been so great in many cases that its failures in others were glossed over.

In 1900 van Laar (32, see also 31) showed that, on account of the strong electrostatic forces between ions, they can not be expected to be independent and to behave as ideal solutes. His theory did not attract enough attention to receive a name. Since it denied the existence of completely independent ions we may call it the theory of "complete association." Later Sutherland (53) and Bjerrum (3) emphasized this point of view, and claimed further that the electrostatic action was enough to account for all the behavior of "strong electrolytes," so that they denied also the existence of un-ionized molecules of the electrolyte. Possibly because it seemed more susceptible to experimental proof, this second conclusion has been so much stressed that the whole theory has been called the theory of "complete dissociation." It is interesting to imagine how different the reception would have been had the emphasis been kept on van Laar's more fundamental idea and the name "complete association" given to the theory.

What was the American attitude at this time? For then American physical chemists formed a compact enough group so that they might be said to have an attitude. They came close to accepting the theory of complete ionization even before Sutherland and Bjerrum. How near can best be shown by quoting from an address given by A. A. Noyes in 1904 (36). "Thus the experimental data fully warrant the statement of the principle that *the optical activity and the color of salts in solution, when referred to equivalent quantities, are independent of the concentration and therefore of the degree of ionization of the salts and are additive with respect to the properties of the constituent ions even up to concentrations where a large proportion of the salt is in the un-ionized state.*"

We shall skip the presentation of experimental data familiar to all of you, but then continue to quote, "If there were no other evidence to the contrary, the existence of this general principle, which is also applicable to many other properties, would almost warrant the conclusion that the salts are completely ionized up to the concentration in question, and that the decrease in conductivity is due merely to a change in migration velocity. But in view of the apparently conclusive evidence against such a hypothesis, we can only conclude that the form of union represented by the un-ionized molecules of salts differs essentially from ordinary chemical combination, it being so much less intimate that the ions still exhibit their characteristic properties, in so far as these are not dependent upon their existence as separate aggregates."

By sufficiently emphasizing "separate aggregates" we might read much into that last sentence, but we shall merely note that the American physical chemists stuck to sane middle ground, accepted neither complete ionization nor a partial ionization measurable by conductance, and devoted their attention to the collection of experimental data and to the development of a rigorous thermodynamics independent of any particular picture. Van Laar was also doing the latter, but while van Laar argued, the Americans taught. In particular, Lewis, by developing rigorous equations which took the same form as the inexact ones of the Arrhenius-van't Hoff theories, developed a large audience capable of applying thermodynamics and understanding solution theories.

The theory of interionic attraction was born into a world most of which accepted without any question the theories of Arrhenius and van't Hoff as developed by Ostwald and Nernst. For eleven years the new theory was a feeble and awkward child. Its father thought well of it, but no one else paid it much attention except on one occasion, and then the attention paid was far from favorable. Almost every child passes through a period of rather obnoxious publicity-seeking when it first discovers that certain words can shock the adult ear. Our young theory was no exception. In its sixth year it passed through what we may call the "swear-word episode" or the Ghosh theory (23).

Then at eleven years there was a sudden change from the feeble, awkward child to an elegant, graceful, and powerful youth. The paper of Debye and Hückel is a much more important event in the life of the interionic attraction theory than its birth itself. Since then the growth has been so rapid and in so many directions that we shall not attempt to be chronological in the rest of our description.

Let us stop first to consider how an electrolyte solution differs from one containing only non-electrolytes. The first difference is that the forces between ions fall off much less rapidly with the distance than forces between neutral molecules; and the second is the duality of an electrolyte solution,—the fact that positive and negative ions must always exist together, and in such quantities that the total amount of negative electricity is the same as the total amount of positive. If any ion is isolated from the rest, the solution is divided into two parts with charges of equal magnitudes but of opposite signs. The first problem of the interionic attraction theory is to determine the distribution of that charge

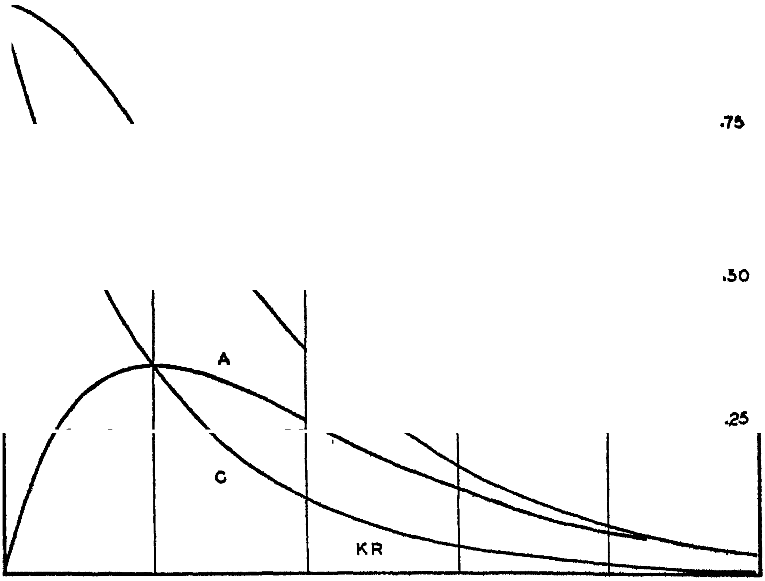

FIG. 1. AVERAGE DISTRIBUTION OF ION ATMOSPHERE

which is not located in the central ion, the charge which Debye calls the "ion atmosphere." It cannot be uniformly distributed throughout space because the total charge, including the central ion, must be uniform. However, it is not closely packed around the central ion.

The average distribution of the ion atmosphere as determined from Debye theory is shown in figure 1, in which the abscissas are the distances from the center of the central ion. For Curve A the ordinates are the fraction of the ion atmosphere contained in a spherical shell of radius R divided by the thickness of the shell. For Curve B the ordinates are the fraction of the ion atmosphere farther from the central ion than R. These are not merely illustrative curves. According to the Debye-Hückel approximation they hold for all values of the concentration, provided that, when the ion atmosphere cannot approach closer than a distance a to the central ion, the unit ordinate for both curves is the value of the B curve for $R = a$, and also that the abscissas be measured as κR, that is, that the unit of length is $1/\kappa$, where κ is the well-known Debye-Hückel function[2]

$$\kappa^2 = \frac{8\pi N\epsilon^2}{1000DkT}\mu$$

The most appropriate measure of the thickness of the ionic atmosphere is the distance at which the A curve reaches its maximum, for more of the ionic atmosphere is there than anywhere else. This distance is $1/\kappa$. We see, however, that almost three-quarters of the atmosphere is at a still greater distance from the central ion. A charge near the central ion has, of course, a greater effect on the potential of the central ion than an equal charge further away. The C curve shows the fraction of the effect of the ion atmosphere on the potential at the central ion produced by that part of the atmosphere farther away than R. This is also accurate for all concentrations provided that the unit ordinate is the value at $R = a$, which is the same in this case as measuring from the inner edge of the ion atmosphere. The contributions of the neighboring parts are relatively large, but there is still an important share contributed by the distant parts of the atmosphere. As the concentration approaches zero this diagram spreads out in terms of real distances, so that the fraction of the effect produced by the atmosphere within any measurable distance is immeasurably small. It is this effect of far distant molecules, particularly at very small concentrations, which makes electrolyte solutions so different from those containing only non-electrolytes.

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[2] N is Avogadro's number, ϵ the electronic charge, D the dielectric constant, k the Boltzmann constant, T the absolute temperature, and μ the ionic strength in moles per liter.

Curve C, if turned upside down and mirror-imaged to negative values of R, also shows the potential energy of the central ion due to its atmosphere. We see at once that the removal of the central ion from its equilibrium position requires work. Let us imagine the central ion to be suddenly obliterated. The ion atmosphere would gradually melt away. The time in which the potential of the atmosphere at its center would fall to 1/e'th part of its original value is called the time of relaxation. It depends upon the mobility of the ions and also upon the distances they have to travel, that is, upon the thickness of the ion atmosphere.

Those effects which depend upon the motion of the ions can be calculated from these two properties of the ion atmosphere—its thickness and its time of relaxation. The first of such effects to studied was the conductance. According to the original treatment of Debye and Hückel (12), or to the correction and extension of Onsager (37), the equivalent conductance decreases with increasing concentration for two reasons. The first, called the time of relaxation effect, comes from the fact that the ion atmosphere of a moving ion always lags behind, so that ahead there is always too little of the opposite charge for equilibrium, and behind there is always too much. The second, called the cataphoresis effect, arises from the fact that the ion must move through a medium bearing the opposite charge and therefore moving in the opposite direction. The success with which this picture explains the experimentally measured conductances in dilute solutions will be treated by other contributors to this symposium.

We shall take time, however, to consider the relation of conductance to frequency and to field strength. When an ion reverses its direction due to the reversal of the external field, its motion is aided by the dissymmetry of the atmosphere rather than hindered. As the frequency increases, the gain at the beginning of each tack compensates for more and more of the loss at the end until, when the frequency is great enough, the ion oscillates about its equilibrium position so rapidly that the ion atmosphere helps as much as it hinders, and the time of relaxation decrease in the equivalent conductance disappears. Since the ion atmosphere is always present, the cataphoretic effect is unchanged. The experimental measurements (45, 46) not only show the qualitative effect predicted by Debye and Falkenhagen (17), but they agree quantitatively with the theory as to the magnitude of the effect and the frequency at which it appears. There is also a phase difference between the potential and the current which appears to macroscopic measuring instruments as an increase in the dielectric constant, which is also predicted by the theory as to both magnitude and dependence upon the frequency.

If an ion moves fast enough it may escape completely from its ion atmosphere, so that both causes of diminished mobility disappear and the equivalent conductance approaches that at zero concentration. The rate of change of mobility with changing speed, that is, with changing field strength, also depends upon the time of relaxation. The measurements of Wien (55) are explained by the calculations from the Debye theory (28). It was hoped that such measurements would give an opportunity of distinguishing between incomplete ionization and the physical interionic attraction, but it appears from the measurements with weak acids (57) that the high fields used can also change the ionization equilibrium.

The viscosity is found to increase as a linear function of the square root of the concentration with a factor depending on the thickness of the ionic atmosphere and its time of relaxation (19, 20), and the most accurate experimental measurements check quantitatively. A similar effect has been calculated for the diffusion of ions (38), but no comparison has been made with experiment.

It is possible to adopt a point of view so strictly chemical as to take no interest in the foregoing properties because they have no influence on chemical equilibria or reaction rates. Even then these results must be considered important on account of the confirmation they give of the Debye picture of the ion atmosphere. Many theories can account for a decrease with increasing concentration of the equivalent conductance and the activity coefficient. Up to the present the theory of a diffuse ion atmosphere is the only one which has accounted for the proportionality to the square root of the concentration; the fact that this theory gives the proportionality constant accurately in both cases is a strong confirmation of its essential correctness; the fact that it also accounts quantitatively for the time effects by taking into account the mobility of the ions and the distances they must travel seems practically conclusive, and gives us much greater assurance in making use of the picture for equilibrium relations.

These equilibrium relations depend upon the thickness of the ionic atmosphere but not upon the time of relaxation; so they are independent of the mobility of the ions. Debye and Hückel showed that in very dilute solutions the change in the electrical contribution to the chemical potential of a salt is proportional to the square root of the ionic strength with a proportionality factor depending only on the temperature, dielectric constant of the solvent, and the valence of the ions. They calculated the effect on the properties which are directly determined by the chemical potentials (or activities) of the salt and the solvent.

Their treatment has been extended to other properties which can be calculated from the variation of the chemical potentials with external conditions: the heat of dilution, for which the proportionality factor depends also on the temperature coefficients of the dielectric constant and of the volume (26, 4, 1, 33, 22, 46); the heat capacity, which depends also on the second temperature coefficients of these variables (39, 10); and the change of volume on dilution, which depends upon the change in chemical potential and upon the pressure coefficients of the dielectric constant and the volume (40, 41). It has also been applied to the surface tensions of salt solutions (54), but those results need reconsideration. The equilibrium properties, applied to steady state conditions, have also been applied to the rates of reactions involving ions (7, 8, see also 50).

Most of these applications will be considered in the papers which follow. We shall content ourselves with noting that the measurements of properties which depend directly upon the chemical potential agree well with the theory, but that the square-root limiting law holds only for small concentrations. As other coefficients are introduced, the theoretical calculations become less certain, and the measurements in dilute solutions less accurate; apparently the deviations from the calculated limiting slope also become greater, and the square-root limiting law appears to hold to higher concentrations.

The later developments which are concerned with the limiting law are attempts to show that the lack of generality of the original treatment does not affect its conclusions. Debye and Hückel treated a model in which the ions are regarded as rigid spheres, all of the same size, differing from the solvent only in the possession of a charge, and not polarizing the solvent around them; their treatment depends upon the expansion of an exponential in a power series and dropping all but the first two terms, and upon rather unorthodox statistical mechanics. Kramers (30), Fowler (21), and van Rysselberghe (44) have attempted to apply more orthodox methods, and their results indicate that the square-root term is unaffected. Gronwall, La Mer, and Sandved (24) show that the use of the complete exponential does not change the square-root term. Debye and Pauling (15) eliminate polarization as a disturbing factor; and Kirkwood and I show that neither unequal size (48) nor lack of spherical symmetry (49) affect the square-root term. The theoretical as well as the experimental evidence for the quantitative correctness of the limiting law has grown continually stronger.

It seems to me that at present the greatest interest is in the more concentrated solutions. No attempt has been made to extend the theory of non-reversible effects beyond the square-root term. On the other hand, the original Debye-Hückel treatment of equilibrium effects showed how the ratio to the square root of the concentration of the non-ideal part of the chemical potential should decrease with increasing concentration, the more rapidly the larger the ions. It was soon found experimentally that many solutions show a much less rapid decrease or even an increase of this ratio. Two explanations have been offered. The first is incomplete ionization. Probably all of us will agree that this is the correct explanation for weak acids and bases, but in general it is not satisfactory. The second method of explanation is to take into account the error of the simple Debye-Hückel picture for close distances of approach of the ions. Stopping the series expansion with the second term as they do is equivalent to assuming that the average total concentration is independent of the distance from the central ion. Figure 2 shows the total number of ions in each spherical shell and the difference between the numbers of negative and of positive ions, first as calculated by the Debye-Hückel approximation, and second as given by the complete exponential at the limit of zero concentration, which

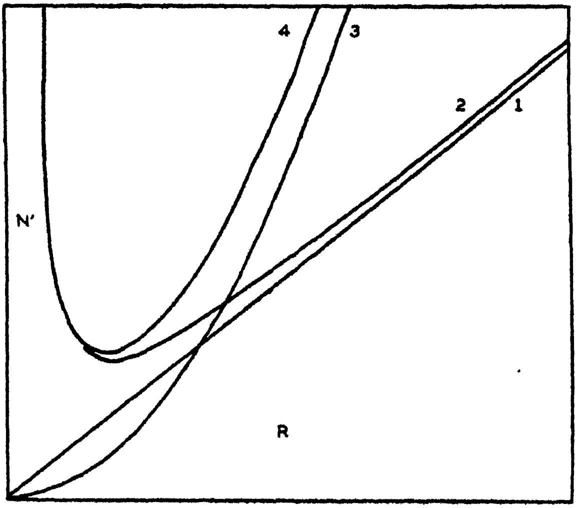

Fig. 2. Ion Atmosphere near Central Ion

also gives the approximate distribution for any small concentration. For very close approach the first approximation is seriously in error. Comparing this figure with figure 1 we see that the reason this error does not affect the limiting law is that in figure 2 the distances are in absolute units, so that for small concentrations this figure represents a slice of negligible thickness from the left side of the first.

Bjerrum (5) was the first to undertake the solution of this problem. He notes that the number of ions in the spherical shells near the minimum in the distribution curve must be very small. When the total concentration is small it is probable that, when one ion is closer than this minimum, all the other ions will be so far away that they may be considered equidistant from the first two. Then a second approximation can be made by treating the number of such pairs by the law of mass action. Bjerrum found that the result depends very little upon just where the outer limit to the pairs is placed, but that it is very sensitive to the inner limit. The correction to the first approximation is very small until the lower limit is half the distance to the minimum. It is interesting to note that this is only one-quarter the distance within which the first approximation gives a negative concentration of ions of the same sign as the central ion, showing that the accuracy of an approximation may be very different for different properties. Bjerrum entitled his paper "Ion Association," and his result has the same form as that for compound formation between the ions. As a consequence many have confused his treatment with incomplete ionization. The application of the law of mass action depends not at all upon the existence as a chemical compound of the ions treated as a pair. It might equally well have been used to determine the number of pairs whose separation is between nine and ten times the equilibrium distance. That the association treated by Bjerrum is part of the general association of electrostatic interionic attraction is shown by the fact that the extent of it depends upon the ionic charge, size, and concentration, the dielectric constant of the solvent and the temperature, but upon nothing else.

Müller (35) attacked the same problem by graphic approximation of the unexpanded exponential. Gronwall and La Mer (24, 25) give an analytical solution to the third approximation of a problem differing from the required one only in the fluctuation terms. The three methods give answers which are practically identical. Although the more physical method of Bjerrum lends itself better to qualitative exposition, there is no question but that the Gronwall-La Mer treatment is to be preferred for quantitative calculation with binary salts, where the convergence is rapid. With unsymmetrical salts there might be an advantage in using the analytical results for the symmetrical case with a theorem of Bjerrum that the electrical contribution to the mean chemical potential of the ions is the same for all solutions for which κa and (z_+z_-/kTa) are the same. For the case where there are two types of ions of the same sign but different sizes there is no solution other than the use of such a theorem.

The calculation of these correcting terms gives a quantitative answer to two criticisms which have been raised against the interionic attraction theory. The first is that at small distances from the central ion the electrical density demanded is greater than the total ion density. We have seen that the correction needed on this account is very small up to distances only one-quarter of that at which the difficulty begins, and it is probable that the correction is calculated to a good approximation even to much smaller distances. The second criticism is that it must be erroneous to use the dielectric constant of the solvent to calculate the mutual energy of two molecules so close together that there are no solvent molecules between them: actually such a calculation leads to only a small error whose effect would be to change slightly the number of pairs close together and so change a little the interpretation to be given to the distance a.

The limiting law and the modification of it at higher concentrations depending upon the size of the ions, including the higher term corrections, we will call the charge-charge effects, because they are calculated upon the assumption that an ion differs from the same volume of the solvent only in the possession of its charge.

Another class of solutions shows a decrease with increasing concentration of the ratio of the non-ideal part of the chemical potential to the square root of the concentration much greater than that calculated by Debye and Hückel. In many cases the non-ideal term even passes through a minimum and then increases to a large positive value. This also has received both physical and chemical explanations. The chemical explanation is that the ions are solvated. The physical explanation is that there is a mutual energy of ions and neutral molecules which can be expressed in terms of the charge and size of the ions and the dielectric constant and volume of the neutral molecules. Debye (13) modified his original derivation of the chemical potential from the electrostatic potential to avoid an error copied from Milner. The new treatment reduces for zero concentration to the form of Born's result (16) for the transfer of an ion from a vacuum to a solution. Debye and McAulay (14, see also 16) have applied this same treatment to ions in mixtures of non-electrolytes with different dielectric constants to explain salting-out effects, and Hückel (27, see also 48) extended the treatment to the action of ions on each other. Since this effect depends upon the charge of an ion and the dielectric properties of another molecule, which may be charged or uncharged, we will call it the charge-molecule effect. Kirkwood has developed the treatment given in our joint paper to obtain a solution for a spherical molecule with any distribution of charges which will reduce many charge-molecule effects to the same basis as the Debye-Hückel approximation for charge-charge effects and should be very useful for unsymmetrical ions. Unfortunately this was done too late for inclusion in this symposium.

Even for symmetrical monatomic ions the properties at high concentrations are very far from being additive for the ions (18). To explain this fact it is necessary to include a third effect. The most probable one is the same type of behavior as that shown by a mixture of non-electrolytes. If the rare gases were soluble enough in water we should expect them to show positive deviations from Raoult's law proportional to the squares of their molal volumes (47). The rare gas type ions appear to show this effect, and for two large ions it is large relative to the electrical effects at moderate concentrations (48). It corresponds to an activity coefficient decreasing with increasing ion concentration. More complex ions, particularly in non-aqueous solvents, might show an increase. We shall call this the molecule-molecule effect because it does not depend at all upon the ionic charges. The theory that such effects are chemical in nature has also been upheld strenuously, but it is now generally abandoned for non-electrolyte mixtures.

We have seen that much of the behavior of ionic solutions may be explained in either of two ways,—chemical or physical. For all effects which depend upon close approach they may be regarded as two ways of looking at the same thing. The simple chemical picture assumes that two molecules which interact with each other to form a compound do not react with a third molecule; the simple physical picture assumes that each interacts with the third as though the other were not there. Generally the truth lies somewhere between the two and may be approximated by improvements on either. For most ionic solutions it appears that the truth lies so much nearer to the simple physical picture that the chemical picture may be objected to as giving a distorted view. Certainly it may be criticized as giving a hazy and indefinite view. This is partly because we have no definition of a simple molecule such that we know what one is in a liquid, and partly because no attempt has been made to correlate the extent of compound formation with any other properties of the reactants. Under these circumstances chemical association is merely another word for an activity coefficient decreasing with increasing concentration, and solvation another word for activity coefficient increasing with increasing concentration. In the present state of knowledge it is greatly to be recommended that, in liquid solutions at least, chemical action be used as an explanation only for effects which cannot be accounted for in other ways.

The other classification seems to me to lead to positive results. It is convenient to think of an ion as an electrical charge superimposed upon a neutral molecule, which acts like other molecules except as its behavior is modified by the fact that it must always accompany the charge. It is certain that non-electrolyte mixtures deviate from the laws of ideal solutions, and that the forces which cause these deviations persist in electrolyte solutions. It is equally certain that, when ions are introduced, new forces come into play which lead to the salting in or salting out of non-electrolytes, and another set of forces which lead to the salting in of ions. We have labelled these three classes: molecule-molecule, charge-molecule, charge-charge.

There appear to be three ways to determine to which class a given effect belongs. The first method is to compare the measured value of some property with that calculated theoretically over a range of concentration of a single substance. The difficulties are that, aside from the square-root limiting law, each of the three classes has the same general behavior: each is proportional to the concentration multiplied by a function which decreases rather slowly with increasing concentration; the form of each function is not very accurately determined because of the approximations which must be introduced; and each depends upon at least one parameter difficult to determine independently. In spite of these difficulties it would be possible, with a slight modification of a method already used (48), to obtain very fair results for the chemical potential of any alkali halide in aqueous solution without using a single measurement on any of these solutions. The method appears less satisfactory for those ions which do not have the noble gas structure, and probably for solvents with a lower dielectric constant than water. The simple methods used thus far are entirely inadequate to account for the behavior of those cases where a proton may shift from one molecule to another, that is, for weak acids and bases. However it is poor science to ignore an effect because we do not know how to calculate it accurately, and we should recognize that all three effects are always present.

The second method is to make the comparison with the same effect for several compounds, preferably including the theoretical calculations. It is desirable that the compounds should be simple enough so that some of their properties may be determined in other ways. This was the method adopted for the study of the alkali halides discussed above. Later in the symposium Prentiss and I are attempting to make a purely objective study of some dilute solutions from this point of view.

The third method is to compare two or more properties of the same solution, for example the change in partial free energy and the corresponding heat content, or the change in free energy and its temperature coefficient. For the charge-charge effect in aqueous solutions the free energy and heat content changes have opposite signs in the limiting law. If the collision diameter is independent of the temperature, the ratio of heat content to free energy increases for the higher terms, and it is physically improbable that the diameter ever changes rapidly enough with increasing temperature to decrease the ratio greatly.

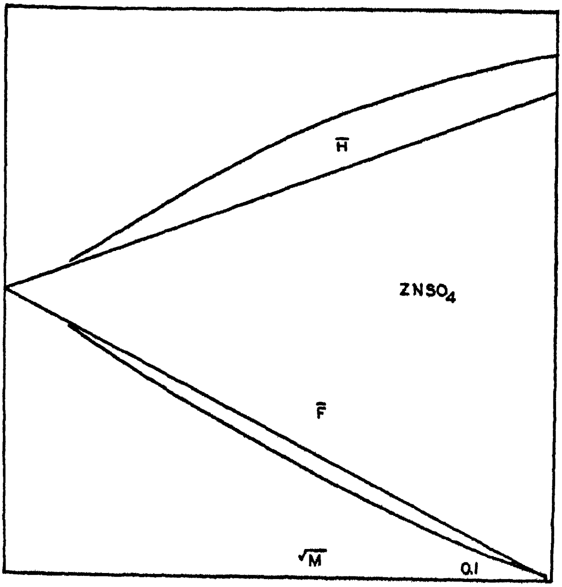

FIG. 3. PARTIAL FREE ENERGIES AND HEAT CONTENTS OF ZINC SULFATE

Theoretically the charge-molecule effect should give a free energy change nearly proportional to the temperature, the ratio decreasing or increasing slightly depending on the change of dielectric constant with the temperature. Experimentally we know that the salting out of non-electrolytes is almost independent of the temperature, increasing slightly in some cases and decreasing in others. Then the heat content change is almost zero.

The molecule-molecule effect can be treated only empirically. For non-electrolyte mixtures we know that the non-ideal free energy change is either nearly independent of the temperature or decreases with increasing temperature; that the heat content change has the same sign as the free energy change and is equal to it in magnitude or larger. This corresponds to the old rule that all dissociations increase with increasing temperature.

Figure 3 shows the two properties for very dilute zinc sulfate solutions (9, 10). It is clear that these meet our specifications for a charge-charge effect, though this appears to be no longer true in more concentrated solutions.

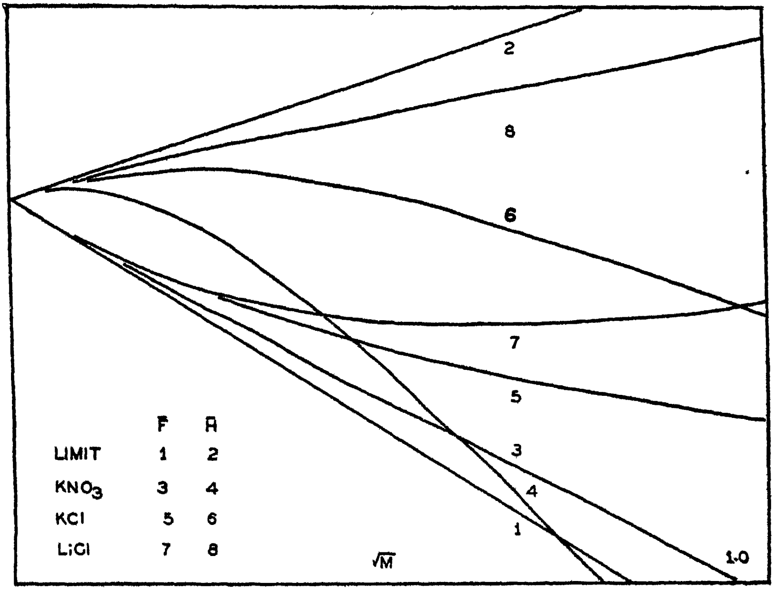

FIG. 4. PARTIAL FREE ENERGIES AND HEAT CONTENTS OF SOME 1-1 SALTS

Figure 4 shows the corresponding effects for three uni-univalent salts. In the more concentrated solutions these must be taken as merely illustrative, for the free energy change is measured at the freezing point (51, 52), and the heat content change at 18°C. (42). For potassium nitrate, the limiting law appears of course as a charge-charge effect, but beyond that the heat content change is also negative and so much larger than the free energy change that the two curves cross. There is obviously a very large molecule-molecule effect. The great excess of heat content over free energy may be explained by a charge-molecule effect of the opposite sign, which contributes to the free energy but not to the heat content.

The fact that there are at least three factors is shown clearly by the lithium chloride and potassium chloride curves. The heat content curve for lithium chloride and the free energy curve for potassium chloride are approximately what we should calculate for the charge-charge effect for either. Then the molecule-molecule effect must be small for lithium chloride, but the great difference in the free energy curve shows a large charge-molecule effect. For potassium chloride on the other hand, the molecule-molecule and charge-molecule effects nearly balance in the free energy change, but the large molecule-molecule effect shown by the heat content change indicates that the charge-molecule effect must also be large.

It is interesting to see how weak acids and bases fit into this classification. The dissociation constants are nearly independent of the temperature, often passing through a maximum between 0°C. and 100°C. That means that the free energy change is nearly proportional to the temperature, and that the heat content change is nearly zero. We should then classify it as a charge-molecule effect, or better as a mixture, perhaps of all three, in which the charge-charge and molecule-molecule effects almost cancel in the heat content change.

It is too early to insist that this classification will be useful in all cases, but there is no question that these results do show the existence of at least three factors. Perhaps the most obvious point to be drawn is that the problem is a very complex one and must be attacked from every possible point of view. It seems to me that very interesting results might be obtained from precision measurements of conductance and its temperature coefficient. There are such measurements, but I find none of great precision. The charge-molecule effects appear not to influence the conductance greatly, but it should be possible to distinguish between charge-charge and molecule-molecule effects. Rudolphi (43) in 1895 suggested an equation which contains the first square-root limiting law for the conductance of strong electrolytes, and classified the salts into those which give constants decreasing with the temperature and those whose constants are practically unchanged. I question whether it would be worth while to analyze existing data by modern methods, but it does seem that advantage should be taken of the great precision now obtainable in conductance measurements.

I have tried to make the story of the past and present of the interionic attraction theory a portrayal of ideas. In so brief a survey of a large field it has been necessary to omit the mathematics necessary to express these ideas precisely, and to discuss the experimental data with which such expression must correspond only when it appears that they would not otherwise be discussed in this symposium. The story of the future will depend much more upon mathematics and experiments. With regard to the experiments it is not difficult to prophesy that we shall continue to have more and better data. To predict the development of a theory, either in ideas or in mathematical treatment, is harder than to predict the weather. We may say that any truly satisfactory solution must wait a development that can express chemical action in precise physical terms and one that can treat a liquid taking into account the existence as molecules of every species present. How long this will be in coming, and whether it will require only an extension of mathematical methods or will need also new physical ideas, are questions which we cannot answer at present.

In the meantime progress will be made by developing different phases of the theory along different lines. It will be desirable to use every available method, and this will lead to some confusion for it will be difficult to avoid counting the same effect twice as expressed in different terms. I believe that the future will not change the results of the theory as it concerns the limiting law. The treatment of more concentrated solutions will doubtless undergo considerable change, though I believe that here also the main lines have now been correctly laid out.

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THE CONDUCTANCE OF AQUEOUS SOLUTIONS OF ELECTROLYTES AND THE INTERIONIC ATTRACTION THEORY

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This paper is a summary of the results of a series of researches carried out at the Rockefeller Institute on the properties of aqueous solutions of electrolytes. The experimental work has consisted mainly in the determination, with the greatest accuracy now attainable, of conductances and transference numbers of such solutions. As will be seen, the interpretation of the results has been made with the indispensable aid of the interionic attraction theory of Debye, Hückel, and Onsager.

As is well-known, Debye and Hückel have demonstrated that an ion in a solution is surrounded by an oppositely charged "ion atmosphere" which for an undisturbed electrolyte is spherically symmetrical around the ion. This ion atmosphere is the net result of the Coulomb forces between the charged ions and the thermal vibrations. The electrostatic attractions and repulsions acting alone would result in a lattice arrangement of the ions, whereas the thermal vibrations tend to break up any regularity in the spatial distribution. By a combination of the Boltzmann and Poisson equations, Debye and Hückel have shown that as a result of these two effects the potential, ψ, around a selected ion is, neglecting higher terms,

$$\frac{\epsilon e^{-\kappa(a-r)}}{Dr\,(1-\kappa a)} \tag{1}$$

in which ϵ is the charge on the ion, a may be regarded as the distance of closest approach of the ions, r is the distance from the center of the ion, D is the dielectric constant, and

$$\sqrt{\frac{8\pi n\epsilon^2}{DkT}} \tag{2}$$

In the latter formula n is the number of ions per cubic centimeter, k is the Boltzmann constant, and T the absolute temperature. This theory has been successful in accounting for the thermodynamic properties of many solutions of electrolytes, at least at moderate concentrations. It is our purpose, however, to discuss experimental tests of the extension of the theory to account for the phenomena observed when a potential gradient is superposed upon those naturally present in the solution of the electrolyte. From the theoretical point of view this added condition results in much complication, and, strictly speaking, the equations which have been derived are only applicable to solutions which are near to infinite dilution.

The primary effect of the superposition of an external potential in, for instance, the measurement of the electrolytic conductance, is to cause a drift of the ions toward the electrodes. This drift, however, brings about at least two retarding effects. One of these is caused by the movement of an ion from the center of its ion atmosphere due to the impressed potential gradient. The atmosphere will adjust itself to such a shift, but not quite instantaneously. A portion of the atmosphere will thus be behind its normal position and will exert an unsymmetrical force on the ion, tending to reduce its rate of motion. This is known as the "time of relaxation effect." The ions are further slowed down by the "electrophoretic effect." This second effect is due to a counter-current of solvent. The magnitude of this retarding effect on the motion of the ions can be obtained by first computing from equation 1 the apparent charge located in the ionic atmosphere in concentric shells (of thickness dr) around an ion and then, by applying Stokes' law to each shell, obtaining the integrated effect of the ion atmosphere on the solvent.

As the result of these considerations Onsager (1) has obtained the following equation for the mobility or equivalent conductance of an ion

$$= \lambda^0 - \left[\frac{(0.9838)(10^6)}{(DT)^{3/2}} w\lambda^0 + \frac{28.95Z}{(DT)^{1/2}\eta}\right]\sqrt{(Z_1 + Z_2)C} \tag{3}$$

λ^0 is the mobility at infinite dilution,
D is the dielectric constant of the solvent,
T is the absolute temperature,
η is the viscosity of the solvent,
Z is the charge carried by the ion (absolute value),
C is the equivalent concentration,
Z_1 and Z_2 are the charges carried by the anions and cations, and λ_1^0 and λ_2^0 are the mobilities at infinite dilution of anions and cations.

$$w = Z_1Z_2 \frac{2q}{1 + \sqrt{q}}; \; q = \frac{Z_1Z_2(\lambda_1^0 + \lambda_2^0)}{(Z_1 + Z_2)(Z_2\lambda_1^0 + Z_1\lambda_2^0)} \tag{4}$$

The first term in the brackets in equation 3 takes account of the time of relaxation effect, and the second term of the electrophoretic effect, both of which decrease the mobility of the ions. For the equivalent conductance, λ, of an ion constituent in a solution of a uni-univalent electrolyte the expression

$$\lambda = \lambda_0 - \left[\frac{5.78 \times 10^5}{(DT)^{3/2}}\lambda_0 + \frac{29.5}{(DT)^{1/2}\eta}\right]\sqrt{2C} \tag{5}$$

in which λ_0 is the equivalent conductance at zero concentration, is thus obtained. This can be put in the simpler form

$$\lambda = \lambda_0 - (\alpha\lambda_0 + \beta)\sqrt{C} \tag{6}$$

For the equivalent conductance of a uni-univalent electrolyte, Λ, the relation is

$$\Lambda = \Lambda_0 - (\alpha\Lambda_0 + 2\beta)\sqrt{C} \tag{7}$$

in which Λ_0 is the limiting equivalent conductance.

In the following we will discuss: (1) the application of this equation to the data obtained in the measurement of the conductances of aqueous solutions of very dilute strong electrolytes;

(2) an empirical extension of the equation which extends its usefulness to moderate concentrations of most strong electrolytes; (3) precise transference data in the light of Onsager's equation; (4) the application of the extended equation to the conductances of individual ion constituents; and finally (5) the interpretation of conductance data on weak electrolytes from the point of view of the interionic attraction theory.

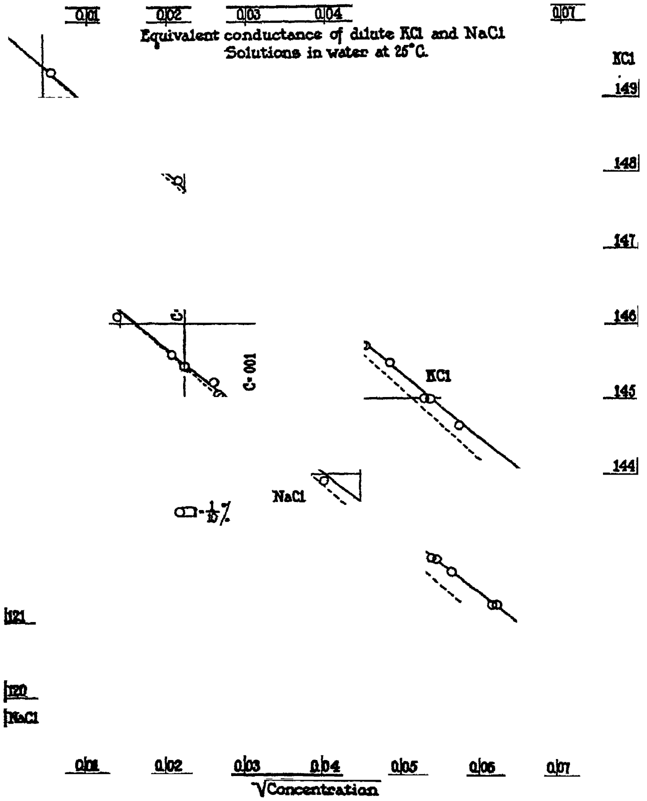

FIG. 1. EQUIVALENT CONDUCTANCE OF DILUTE POTASSIUM CHLORIDE AND SODIUM CHLORIDE SOLUTIONS IN WATER AT 25°C.

1. VERY DILUTE SOLUTIONS OF STRONG ELECTROLYTES

In Onsager's derivation of equation 7 it is assumed that the ion concentration is very low. A test of its validity as a limiting expression must be sought in measurements on very dilute solutions. One of us (T. S.) has made a study, the details of which are given elsewhere (2), with the result that determinations of the conductances of salt solutions as dilute as 0.00003 N have been measured with an accuracy of about 0.02 per cent. For an account of the many experimental difficulties that had to be overcome in attaining this accuracy we will refer to the original paper (2). Here we will only concern ourselves with the results. Some of these, for typical electrolytes, are plotted in figures 1 and 2. In the first of these the measured equivalent conductances of dilute sodium and potassium chloride solutions are plotted against the square root of the concentration. Many years ago Kohlrausch found empirically that a straight line would result from such a plot. It is, however, the distinguishing feature of Onsager's theory that it predicts the slope of the line. This computed slope is $(\alpha\Lambda_0 + 2\beta)$ of equation 7 and is shown on the plots by the dotted line. It will be observed that up to about 0.001 N this theoretical slope and a line through the experimental points agree within the very small

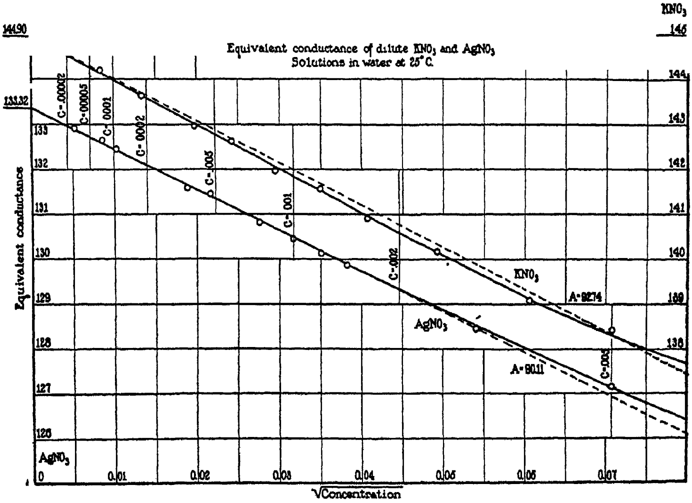

FIG. 2. EQUIVALENT CONDUCTANCE OF DILUTE POTASSIUM NITRATE AND SILVER NITRATE SOLUTIONS IN WATER AT 25°C.

experimental error. There is, however, a real deviation upward of the experimental curve which apparently begins in the most dilute solutions. This deviation is typical of that shown by most binary electrolytes and is, by the way, in the reverse direction to that which would be expected from incomplete dissociation. The behavior shown in figure 2 is much less frequently observed. It will be seen that the data for silver nitrate show no deviation whatever from the straight line predicted from Onsager's theory up to a concentration of 0.002 *N* and that the curve for the measurements on potassium nitrate lies below the limiting slope in the region of very dilute solutions but crosses it at about 0.005 *N*. It is, however, clear from these data and from others already published which are equally striking that the Onsager equation is the limiting expression to which an equation representing the measured conductances must reduce for very low concentrations.

2. MODERATE CONCENTRATIONS OF STRONG ELECTROLYTES

It is evident therefore that the equation describing the equivalent conductance of strong electrolytes at higher concentrations than those considered in the previous section will be one that reduces to the Onsager equation in the limit. According to a recent paper by Onsager and Fuoss (3) the extension of the equation which would follow if the approximations involved in the limiting expression were not made would probably involve a term of the form $BC \log C + DC$ (in which B and D are constants) The mathematical difficulties of such an extension are, however, considerable. Onsager has made use of an extension of the form:

$$\Lambda = \Lambda_0 - (\alpha\Lambda_0 + 2\beta)\sqrt{C} + KC \tag{8}$$

in which K is an empirical constant. This procedure increases the usefulness of the equation only to concentrations of about 0.01 *N*. One of the authors (T. S.) has, however, suggested an extension of the equation which reproduces the experimental results, almost within the experimental error up to nearly 0.1 *N* (4). This equation has the form:

$$\Lambda_0 = \frac{\Lambda + 2\beta\sqrt{C}}{1 - \alpha\sqrt{C}} - BC \tag{9}$$

in which α and β have the same values as in equation 7 and B is an empirical constant. If the term BC is zero, this is identical with Onsager's expression (equation 7). The constant B can be readily obtained by plotting values of

$$\Lambda'_0 = (\Lambda + 2\beta\sqrt{C})/(1 - \alpha\sqrt{C})$$

against the concentration C. The result in the normal case is a straight line with a slope equal to B and an intercept equal to Λ_0. Some typical examples of such plots from the work of this laboratory are shown in figure 3. It is an interesting fact, and one that may prove to have theoretical importance, that for such normal cases the value of B is always within 15 per cent of the theoretical coefficient of $\sqrt{C}$, i.e., $(\alpha\ \Lambda_0 + 2\ \beta)$. A certain number of electrolytes, two of which (silver nitrate and potassium nitrate) have been considered in the previous section, give curves rather than straight lines when their equivalent conductances are treated in the manner just described. These substances are abnormal in at least one other respect, as we will see in the next section.

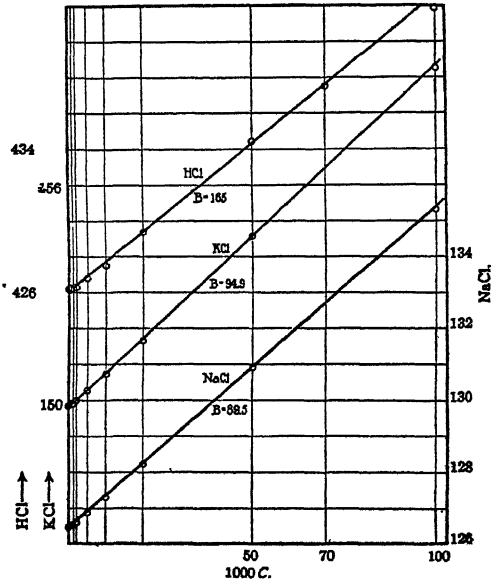

FIG. 3. THE VARIATION OF Λ'_0 WITH THE CONCENTRATION

In summary then we have shown that up to about 0.001 N the equivalent conductances follow Onsager's equation within the experimental error. Above that concentration the data for most electrolytes can be expressed to about 0.07 N with an equation involving only one empirical constant in addition to the limiting conductance, Λ_0.

3. THE INTERPRETATION OF TRANSFERENCE DATA

One of the activities of this laboratory, over a number of years, has been the determination, by means of the moving boundary method, of transference numbers of electrolytes. Recently the accuracy of these determinations has reached very nearly that of the best conductance measurements, or about 0.02 per cent. An extended account of the method has recently appeared in This Journal (5). Until recently transference measurements which were scattered and of doubtful accuracy have had but little influence in connection with theories of solutions of electrolytes. We feel the results of our measurements must be incorporated into any theory which may be formulated in the future. It was one of the weaknesses of the Arrhenius theory that it postulated no changes of the transference number with concentration. Correspondingly, it is a strength of the present theories that they call for such variations, and that they are in the direction and of magnitudes actually observed. Since the transference number T is equal to the ion mobility λ divided by the equivalent conductance Λ, a limiting expression for the change of the transference number with the concentration may be obtained simply by dividing equation 6 by equation 7 (see Dole (6)). On this basis it is readily shown (7) that the Onsager theory requires that the curve obtained by plotting the transference number of the positive ion, T_+, against the square root of the concentration should go into the axis of zero concentration with the slope

$$\left(\frac{dT_+}{d\sqrt{C}}\right)_{C=0} = \frac{T_+^0 - 1}{2\Lambda_0}\beta \qquad (10)$$

In this equation T_+^0 and Λ_0 are the limiting cation transference number and equivalent conductance of the salt respectively, and

β is the constant of the Onsager equation occurring in equation 7. Thus the limiting value of the change of the cation transference number with the change of $\sqrt{C}$ is seen to be proportional to the variation of the number from 0.5 and to be inversely proportional to Λ_0. A test of the validity of equation 10 as a limiting expression is given in figure 4, in which points representing the actual transference measurements are plotted against the square root of the concentration. From the ordinate representing the limiting value of each transference number (which can be accurately computed by a method we will presently discuss), a straight line is drawn with a slope computed from equation 10. It will be observed that smooth curves passed through the observed points

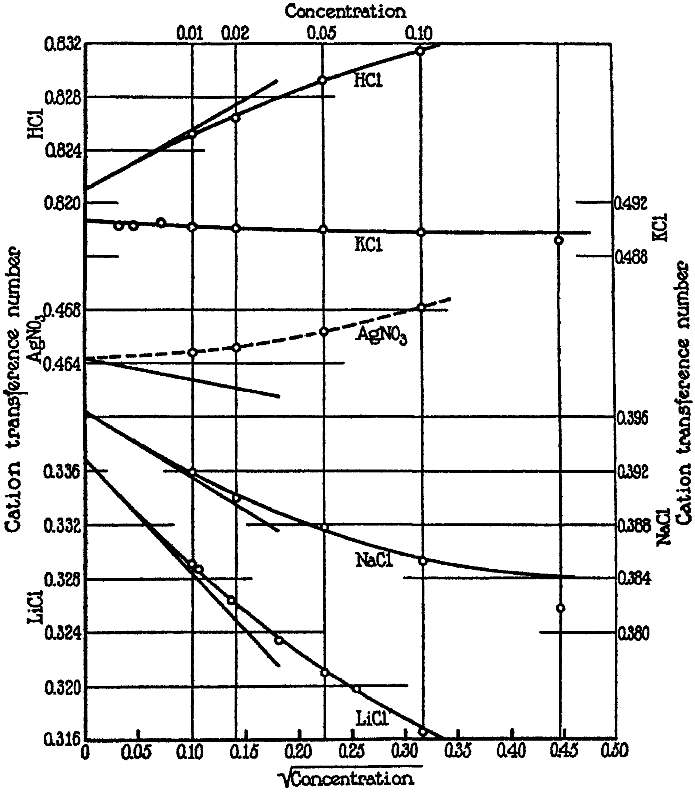

FIG. 4. TRANSFERENCE NUMBERS AS FUNCTIONS OF THE CONCENTRATION

merge into these straight lines as the concentration decreases. In the case of potassium chloride the observed and computed lines are identical. Other examples of the same kind could be cited from the data we have at hand. A marked exception to the rule is also shown on the plot. This is the data on silver nitrate, in which the observed variation of the transference number with the concentration and the computed limiting variation have opposite signs. A somewhat similar behavior has also been observed in the case of potassium nitrate. The exceptional behavior of the conductances of these two substances has already been commented upon. It would appear, therefore, that except for the data on several substances suspected to be abnormal, the transference number measurements provide excellent support to the interionic attraction theory of strong electrolytes.

4. THE CONDUCTANCES OF INDIVIDUAL ION CONSTITUENTS

The validity of Kohlrausch's law of independent ion mobilities

By multiplying the equivalent conductance, Λ, of a salt at a given concentration by the value of the transference number, T, measured at the same concentration, a value of the equivalent conductance of the corresponding ion constituent may be obtained. These data may be conveniently considered in the light of Shedlovsky's extension of the Onsager equation. For a single ion constituent this equation is:

$$\lambda_0 = \frac{\lambda + \beta\sqrt{C}}{1 - \alpha\sqrt{C}} - bC \qquad (11)$$

in which λ ($= T\Lambda$) is the equivalent conductance of an ion constituent and λ_0 is its value at infinite dilution. The other terms have the same significance as in equation 6. Here again we can study the data by observing the trend of values of

$$\lambda'_0 = \frac{\lambda + \beta\sqrt{C}}{1 - \alpha\sqrt{C}}$$

with the concentration C. Figure 5 is a plot of this kind representing the results for the potassium ion constituent from four different salts. Although we expect to discuss these results and others of the same type in detail in a later publication, several facts are evident from a casual inspection of the plot. In the first place the data for a given salt are seen to fall on a smooth curve which is nearly a straight line. All the curves converge to a single point on the axis of zero concentration. This is obviously the limiting value λ_0 of the conductance of the ion constituent in question. Furthermore, although the curves for the potassium ion from different sources diverge at moderate concentrations their values agree, probably within the experimental error up to about 0.01 normal. This means that Kohlrausch's law of independent ion mobilities is valid to that concentration. An exception is the λ'_0 value of potassium ion from potassium nitrate, which here again shows its abnormality. This test of the law of independent ion mobilities is essential for our work on weak electrolytes to be considered in the following section.

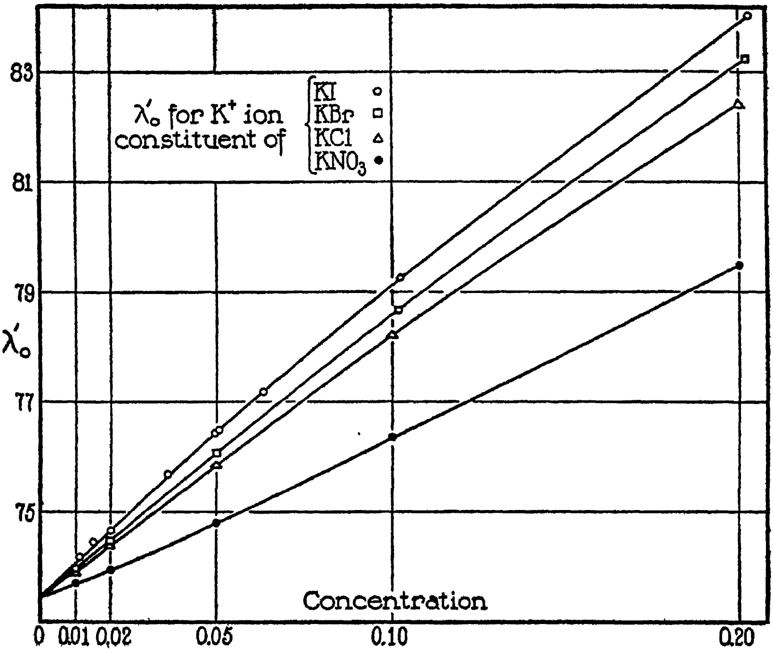

FIG. 5. THE VARIATION OF λ'_0 WITH THE CONCENTRATION

From data such as those plotted in figure 5 it has been possible to prepare table 1, which gives values of the limiting conductances, λ_0, of some common ion constituents. The figures in this table, which are based entirely on the work of this laboratory (8), are not dependent, as were earlier tables, on a single transference number, but, in the case of the chloride and potassium ions, are consistent with four series of transference and conductance measurements. The limiting values of transference numbers used in the previous section may obviously be obtained from the data in this table. Thus the limiting transference number of the lithium ion in lithium nitrate may be found by dividing the λ_0 value for lithium by the sum of the values for the lithium and nitrate ions.

TABLE 1

Limiting ion conductances at 25°C.

CATIONS		ANIONS	
K^+	73 50	Cl^-	76.32
Na^+	50.10	NO_3^-	71.42
H^+	349.72	CH_3COO^-	40.87
Ag^+	61.90		
Li^+	38.68		

The ionization of solutions of weak electrolytes

According to the "classical" dissociation theory, weak electrolytes were found to follow the law of mass action (known in this case as the "Ostwald dilution law") in their ionization, whereas strong electrolytes were found to depart markedly from that relation. This was the familiar "anomaly of the strong electrolyte." The many ingenious attempts that were made to overcome this difficulty were not successful as long as Arrhenius' assumption concerning the computation of the degree of dissociation was uncritically accepted. According to this assumption the degree of dissociation is equal to the conductance ratio, Λ_c/Λ_0, in which Λ_c is the equivalent conductance at the concentration c and Λ_0 is the equivalent conductance at infinite dilution. It can readily be shown that degrees of dissociation can be obtained in this way only if the ion mobilities do not change with the concentration. In an earlier section we have, however, given evidence that the change of conductance of most strong electrolytes with concentration can be accounted for on the assumption that they are completely dissociated and that interionic attractions which increase with the ion concentration produce decreases in the mobilities of the ions. Arrhenius' assumption cannot, therefore, be true even for weak electrolytes, since the ion concentrations change, although slowly, with the total concentration. It was this relatively slight change of the ion concentration with the concentration of weak electrolytes which was partly responsible for the apparent validity of Ostwald's dilution law. From recent studies (9, 10, 11) it will be shown that the ionization of weak electrolytes follows the law of mass action if (a) in computing degrees of ionization allowance is made for the changes of ion mobilities with ion concentration, (b) certain strong electrolytes can be assumed to be completely dissociated, and (c) the activities of the ions follow the Debye-Hückel relations, at least in dilute solution.

For the ionization of a weak acid, $HAc = H^+ + Ac^-$, the law of mass action is correctly stated in the form:

$$K = \frac{(H^+)\,(Ac^-)}{(HAc)} = \frac{C\alpha^2\gamma_i^2}{(1-\alpha)\gamma_u} \tag{12}$$

in which K is the thermodynamic ionization constant, the parentheses represent activities of the components enclosed, α is the degree of dissociation, and γ_i and γ_u are the mean activity coefficient of the ions and the activity coefficient of the undissociated portion, respectively. Since the undissociated portion is uncharged it can be assumed in dilute solution to be a normal electrolyte with an activity coefficient of unity, and equation 12 can be put in the form

$$K = K'\gamma_i^2 \tag{13}$$

in which K' is equal to $C\,\alpha^2/(1-\alpha)$. However, as the ion concentration $C\,\alpha$ must change with concentration and with it the ion mobilities, we cannot accept the ratio Λ_c/Λ_0 as a measure of the degree of dissociation α. A correct degree of dissociation can be obtained from the ratio of the measured equivalent conductance to the equivalent conductance *of the completely dissociated electrolyte at the same ion concentration.* If the latter quantity is represented by Λ_e the correct degree of dissociation α is:

$$\alpha = \Lambda_c/\Lambda_e \tag{14}$$

Since it has been shown in the previous section that Kohlrausch's law of independent ion mobilities holds accurately, up to say 0.005 N, equivalent conductances are additive at a given, low, ion concentration, so that values of Λ_e of the acid HAc can be computed from the following relation

$$\Lambda_{e_{\mathrm{HAc}}} = \Lambda_{\mathrm{HCl}} - \Lambda_{\mathrm{NaCl}} + \Lambda_{\mathrm{NaAc}} \tag{15}$$

The use of equations 14 and 15 implies that all the electrolytes involved are substantially completely dissociated at the concentrations at which they are used. This seems to be a safe assumption, at least for dilute solutions, for salts which follow Shedlovsky's equation. Our experiments have shown that the salts of the weak acids that we have studied (acetic and chloroacetic) as well as hydrochloric acid and the alkali halides belong in this group. With values of Λ_e at a series of concentrations we can proceed to obtain degrees of dissociation α. Since the ion concentration is αC the correct value of Λ_e cannot be found until α is known. The computation can, however, be made by means of a short series of approximations, and is facilitated if Λ_e is expressed as a function of the concentration in the form of equation 9.

With these values of the degrees of dissociation at hand it is possible to compute a series of values of K'. These are, however, not constant but are found to vary with the concentration. If equations 12 and 13 are valid this is to be expected, since the activity coefficient γ_i varies with the ion concentration. As is well-known, Debye and Hückel have derived the following limiting relation

$$-\log \gamma_i = A\sqrt{C\alpha} \tag{16}$$

connecting the activity coefficient γ_i with the ion concentration $C\alpha$. In this expression A is a constant (with the value of 0.5065 at 25°C.) and depends upon the temperature, the dielectric constant, and universal constants. The data we have obtained on the conductances of acetic and chloroacetic acid, together with those on the strong electrolytes which are necessary to compute values of K' have made it possible to test the validity of equation

12 and thus the fundamental postulates of the interionic attraction theory. Equation 13 may be put in the form

$$\log K = \log K' + \log \gamma_i^2 \tag{17}$$

and utilizing equation 16

$$\log K = \log K' - 2A\sqrt{C} \tag{18}$$

Thus the logarithms of the K' values, computed as described above, when plotted against the square root of the ion concentra-

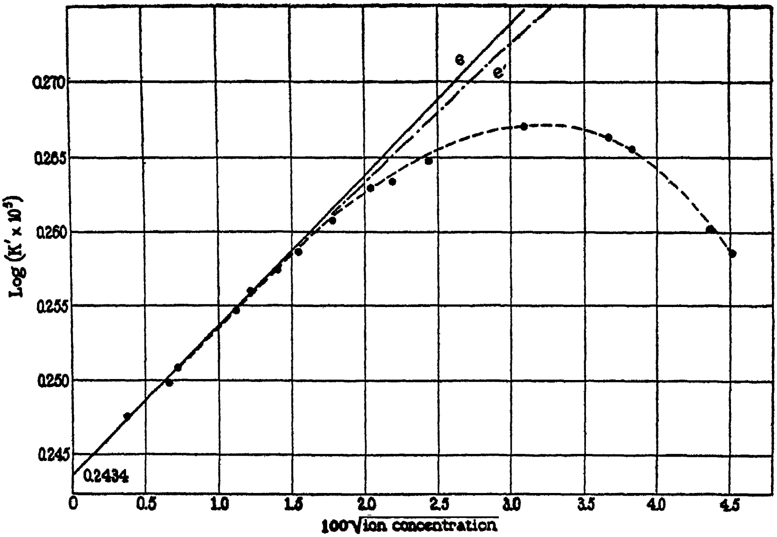

FIG. 6. THE STOICHIOMETRIC "CONSTANT" OF ACETIC ACID AS A FUNCTION OF THE CONCENTRATION

tion should (within the range of validity of equation 16) lie on a line with the slope $2A$ and an intercept equal to $\log K$. A plot from our data on acetic acid (figure 6) indicates that this is accurately true for the more dilute solutions investigated. In this plot the solid line e has the slope 2×0.5065 as demanded by the theory.

The value of the thermodynamic ionization constant K (1.753×10^{-5}) obtained as the intercept at zero concentration on this plot is particularly interesting since we have independent evidence that it is correct. Harned and Ehlers (12) have obtained, by a quite independent method, the value 1.754 × 10^{-5}). Their method involved the measurement of the potentials of galvanic cells without liquid junctions.

A similar plot made from computations based on the data we have obtained recently on the stronger acid, chloroacetic acid, is given in figure 7. By comparing the scales of abscissae on this and the preceding figure it will be seen that for the chloroacetic acid the experimental points lie on the line representing the limiting law to a considerably higher ion concentration, but that otherwise the shapes of the two curves are similar.

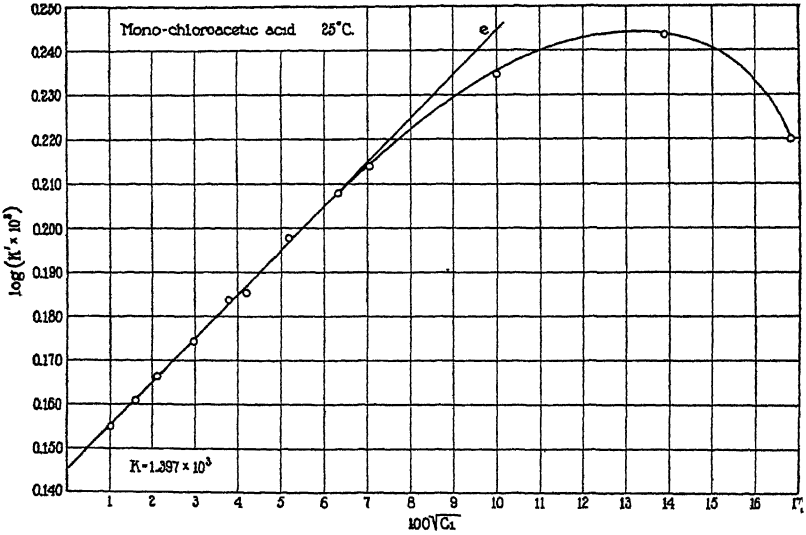

FIG. 7. THE VARIATION OF THE STOICHIOMETRIC "CONSTANT" OF CHLOROACETIC ACID WITH THE CONCENTRATION

The curves through the experimental points in figures 6 and 7 depart more abruptly from the line representing the limiting equation than would be expected from measurements on strong electrolytes. A correction for the size of the ions (assuming the reasonable value of 4 Ångström units from crystal structure data) leads only to the line *e′* in figure 6. The large deviations are undoubtedy due to a change of the properties of the solvent (a "medium effect"), arising from the fact that as the concentration is progressively increased there is an accumulation of undissociated acid in the solution. This effect will be discussed more fully in another communication.

SUMMARY

The conclusions from this study may be outlined as follows.

The conductance measurements on very dilute solutions (from 0.00003 *N* to 0.001 *N*) of strong electrolytes are in accord, within a small experimental error, with the interionic attraction theory of Debye, Hückel, and Onsager.

With an additional empirical term, Onsager's equation can be modified to express the results of conductance measurements on most strong uni-univalent electrolytes to about 0.07 *N*. The constant of this extra term may prove to have theoretical significance as interesting regularities have been observed. The data on certain salts, however, show decided deviations from this semi-empirical equation.

The results of precision measurements of transference numbers show changes with concentration that are in accord with the interionic attraction theory, except, so far as measurements have been made, in the cases in which deviations are observed from the semi-empirical equation just mentioned.

By combining conductance and transference measurements Kohlrausch's law of independent ion mobilities has been found to be strictly true in the limit, and almost within the experimental error up to 0.01 *N*. Above 0.01 *N* the conductance of a given ion constituent depends somewhat on the nature of the oppositely charged ion. The results for the separate ion constituents can, however, be expressed by means of a semi-empirical equation similar to that mentioned above.

The results of precision measurements on conductances of solutions of the weak electrolytes, acetic and chloroacetic acids, have been interpreted in the light of the interionic attraction theory. For the dilute solutions a thermodynamic ionization constant is obtained if the degrees of ionization are computed by a method which allows for changing ion mobilities, and allowance is made for variation of activity coefficients according to the Debye-

Hückel relation. At higher concentrations there is a "medium effect" which arises, in large part at least, from the accumulation of undissociated acid as the concentration is increased.

That the true value of the thermodynamic ionization constant is obtained by the method outlined above is shown by the close check of our value for acetic acid, 1.753×10^{-5}, with the value 1.754×10^{-5} recently obtained by Harned and Ehlers (12), using a quite independent method involving concentration cells without liquid junctions.

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INDICATOR STUDIES OF ACIDS AND BASES IN BENZENE

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In the days before the electrolytic dissociation theory was developed, the term "acid" implied a corrosive substance with a sour taste which would turn blue litmus red when tested in dilute aqueous solution. The term "base" meant the residual substance remaining after the volatilization of the acid constituent, which was bitter, would turn red litmus blue, and was capable of neutralizing the properties of acids.

The ionization theory as developed by Arrhenius and Ostwald introduced the principle that these properties were dependent upon dissociable hydrogen and hydroxyl radicals. The remarkable success which the theory achieved in explaining the behavior of weak acids and bases in particular by correlating their conductance ratios with their catalytic effects, for example, on the inversion of cane sugar by acids or the saponification of esters by bases, convinced most chemists that their older empirical statements of the strength of acids and bases could be simply yet adequately replaced by statements of the concentration of hydrogen ion. Thus, an acid became a substance that gives on dissociation hydrogen ion and an anion; a base, one that gives hydroxyl ion and a cation.

As long as attention was restricted to dilute aqueous solution, these concepts sufficed. However, when we enter the realm of non-aqueous solvents, we are immediately confronted with two questions: What is meant by acidity in a solvent in which the acid or base does not ionize perceptibly, as is the case in solvents like benzene? What do we mean by the term "base" when the substance and its solvent lack hydroxyl radicals?

In 1923 Brönsted (1b) and Lowry (2) proposed, independently of each other, a scheme which greatly simplifies the answers. They define any substance as an acid which is capable of dissociating a proton, and correspondingly, define as a base any substance which will associate a proton. Thus:

$$\text{Acid} \rightleftarrows \text{Base} + \text{Proton} \tag{1}$$

The scheme has the following advantages:

(1) Acid properties are ascribed to one factor—the ability to give up protons; basic properties, to the ability to accept protons. Unless the recently discovered neutron and positron should prove to be important in ordinary chemical changes, the unique properties of minute size and extraordinary mobility possessed by the proton are paralleled only by that of the electron in oxidation-reduction equilibria, where the corresponding scheme is

$$\text{Reductant} \rightleftarrows \text{Oxidant} + \text{Electron} \tag{2}$$

These definitions thus embrace the most fundamental processes in ordinary chemical changes and do so by employing only fundamental concepts of the structure of matter.

(2) The definition is independent of the solvent, so that it is unnecessary to redefine the term "base" on passing to new solvents, as is customary in many existing systems.

(3) Hydroxyl ion loses its exalted position as the unique carrier of basic properties, which position it acquired only because of the frequency with which aqueous solutions are encountered.

(4) Acids and bases are not restricted to electrically neutral molecules. The only restriction is that the base possesses one less positive charge than its conjugate acid.

Properties like freezing point depression, hydrogen electrode potentials, and indicator colors involve equilibrium states and are, therefore, closely correlated for thermodynamic reasons. On the other hand, properties like the conductance ratio, and hydrogen and hydroxyl ion catalysis are not determined by reversible processes. Consequently when it was demonstrated in dilute aqueous solution that there was a close correlation between such thermodynamic and non-thermodynamic properties, it was tacitly assumed that a similar correlation would hold without change when the acids or bases were dissolved in other solvents (7).

Thus, the classical theory held that a solution like that of hydrogen chloride in benzene should not have the properties of an acid, since it failed to conduct electricity and at best reacted very slowly with metals and carbonates. The experimental work of Hantzsch (3), of Brönsted (1), and of Hall and Conant (5) has been primarily responsible for demonstrating that this assumed parallelism between thermodynamic and non-thermodynamic properties does not hold on changing the solvent. The lines of evidence which demonstrate that the classical consideration of acids and bases must be profoundly modified if they are to be applied to non-aqueous solvents and even to certain properties of aqueous solutions (see (2) below), are as follows: (1) properly chosen indicators respond promptly to additions of acids and bases when dissolved in solvents like glacial acetic acid (5) or benzene (1e, 6), whereas the conductivity indicates extremely low ionization; (2) acid (or basic) catalysis is produced by undissociated acids (or bases) (1d), the catalysis being dependent primarily upon the facility with which protons can be transferred from catalyst to substrate (or vice versa); (3) the degree of dissociation as indicated by the conductance ratio in any given solvent depends not only upon the dielectric constant but also upon the extent to which the proton of the acid is transferred to basic molecules in the system (1c).

These results emphasize the distinction that must be drawn between extent of dissociation and acidity when comparison is made in different solvents. To say that a solution is highly acid does not necessarily imply that the concentration of hydrogen ions, behaving as particles osmotically independent of the other constituents of the solution, is large. Instead, the term "acidity" requires only a knowledge of the reversible work of transferring hydrogen ions from the given medium to some standard of reference. The hydrogen electrode potential is thus the logical (1b, 1c) measure of acidity when this quantity can be freed from the perplexing complications of liquid junction potentials and individual ion activities (1f).

The extent of dissociation, on the other hand, is conditioned by all the factors which regulate the separation of ions, the dielectric constant being particularly important in this connection. The reciprocal rôles of the solvent and solute in the ionization process can be interpreted most clearly by recognizing their interaction as an equilibrium between two conjugate acid–base systems with the elimination of the proton as an independent entity.

$$\begin{array}{llll} \text{Acid}_1 & + \text{Base}_2 & \rightleftarrows \text{Acid}_2 & + \text{Base}_1 \\ HCl & + H_2O & \rightleftarrows H_3O^+ & + Cl^- \\ H_2PO_4^- & + OH^- & \rightleftarrows H_2O & + HPO_4^{=} \\ HAc & + NH_3 & \rightleftarrows NH_4^+ & + Ac^- \\ H_2O & + NH_3 & \rightleftarrows NH_4^+ & + OH^- \end{array} \tag{3}$$

BENZENE AS A SOLVENT

Ordinarily the solvent, by virtue of its own acid or basic properties, operates as the second acid–base system and thus facilitates ionization, a property most highly developed in water because of its amphoteric character. Benzene, on the other hand, presents an extreme contrast to water. Owing to the absence of acid and basic properties, benzene can act only as an inert diluent; consequently a second acid–base system must always be added to produce and define the equilibrium. By the same token, the range of acidity possible in benzene should be greater and depend only upon the intrinsic character of the acids and bases added, i.e., not be limited as in the case of water by the acid strength of H_3O^+ and the basic strength of OH^-. The low dielectric constant ($D = 2.28$) introduces complications which are not encountered in water, one of the most important being the greatly increased association of ions as a result of the electric forces (8b). The significant problem in such a solvent may be stated as follows: How constant will the relative acidities of a series of acids of the same electric charge type remain on transferring from water to benzene?

Were it possible to refer hydrogen electrode potentials measured in different media to a common scale, new definitions of acidity would be unnecessary. In the present state of knowledge regarding individual ionic activities and junction potentials, the strength of any acid, HA, can be measured most satisfactorily by the extent to which it reacts with any one base, B, chosen as standard for the solvent in question by employing the relation

$$\left[\frac{\mathrm{HB}}{\mathrm{B}}\right]\left[\frac{\mathrm{A}}{\mathrm{HA}}\right] = \frac{K_{\mathrm{HA}}}{K_{\mathrm{HB}}} = K \qquad (4)$$

valid for a constant environment. The brackets designate the *concentrations* of the components. K is then one measure of the acidity and depends mutually on the strength of HA as an acid (K_{HA}) and on the strength of HB as an acid (K_{HB}).

$$a_{\mathrm{H}^+} \equiv K_{\mathrm{HA}}\left[\frac{\mathrm{HA}}{\mathrm{A}}\right] = K_{\mathrm{HB}}\left[\frac{\mathrm{HB}}{\mathrm{B}}\right] \qquad (5)$$

The proton activity a_{H^+} of the solution may be defined by equation 5 and measured in terms of whichever acid–base system (HA:A) or (HB:B) is most convenient.

By the aid of equation 4, Brönsted (1e) arranged a series of twenty-four acid–base systems in accordance with their decreasing acid strengths in benzene (see reference 5c). No numerical data were presented and he emphasized that his results were entirely provisional.

EXPERIMENTAL

To explore to what extent salt formation may proceed in benzene, we (7) determined the changes in conductivity produced by alternate additions of trichloroacetic acid and the soluble base, diethylamine. A special low resistance cell was used and the conductance measured by noting the deflections on a Leeds and Northrup type 2500 galvanometer when the cell and galvanometer were placed in series in the 110-volt direct current line, a method since established by Kraus and Fuoss (8a) as being entirely reliable when the conductivity is extremely minute.

The equivalent conductance is of the very low order of 10^{-11} to 10^{-9} reciprocal ohms, and depends upon concentration in a peculiar manner (8a, 8b). The minimum conductance, however, occurred at points corresponding to equal additions of acid and base and clearly indicates that a prompt reaction occurs.

Electrometric titrations

We next investigated the change in hydrogen electrode potential by the use of a quinhydrone electrode cell of the type

	Trichloroacetic acid (0.165 M)	Trichloroacetic acid (0.165 M)	
	Diethylamine (0.0413 M)	Diethylamine (x)	
Pt	Tetraisoamylammonium iodide (saturated)	Tetraisoamylammonium iodide (saturated)	Pt
	Quinhydrone (a)	Quinhydrone (a)	

For the standard half-cell on the left we used trichloroacetic acid partly neutralized by diethylamine, and on the right side diethylamine was added progressively to the trichloroacetic acid. To improve the conductivity, the benzene was first saturated with tetraisoamylammonium iodide, a salt which is moderately soluble in this solvent.

The E.M.F. was measured by charging a 10-microfarad condenser and discharging it through a ballistic galvanometer. In dry weather the E.M.F. can be determined to less than one millivolt. Typical titration curves were obtained which showed that the trichloroacetic acid system is 0.43 volt more acid than the diethylammonium system, while the monochloroacetic acid system is 0.35 volt more acid, relative to the same standard.

FORMULATION OF INDICATOR RESULTS (9)

(*a*) *Ideal case*

Consider an acid, HA, a very much weaker acid, HB, and an indicator, HI, dissociating to their conjugate bases, A, B, and I. Starting with a solution of the acid HA with a small but constant amount of indicator present, the reaction which occurs as the base B is added is HA + B = HB + A. The indicator must also adjust its dissociation with the change in hydrogen ion activity, thus: HA + I = HI + A. From equation 5

$$\log\left[\frac{\mathrm{A}}{\mathrm{HA}}\right] = \log\left[\frac{\mathrm{I}}{\mathrm{HI}}\right] - pK_{\mathrm{HA}} + pK_{\mathrm{HI}} \tag{6}$$

Experimentally $\left[\frac{\mathrm{I}}{\mathrm{HI}}\right]$ is measured with a colorimeter. For the ratio $\left[\frac{\mathrm{A}}{\mathrm{HA}}\right]$, we assume that the neutralization reaction goes practically to completion, as indicated by the conductivity and electrometric titrations; i.e., the added base B must be strong enough to produce a quantitative conversion, so that the ratio is given by the amount of base added, divided by the amount of un-neutralized acid remaining.

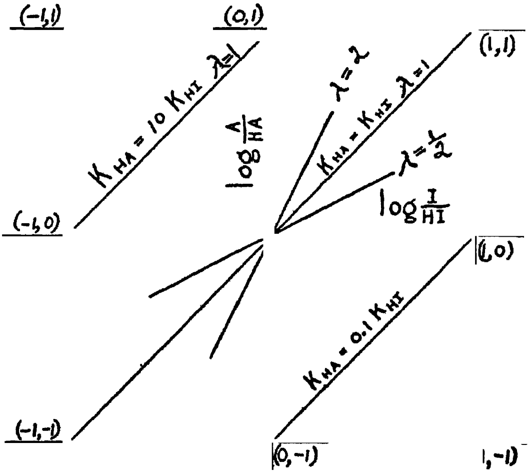

FIG. 1

By plotting log $\left[\frac{\mathrm{A}}{\mathrm{HA}}\right]$ against log $\left[\frac{\mathrm{I}}{\mathrm{HI}}\right]$ as in figure 1, a family of parallel lines with unit slopes results, three members of which have been selected to cut the log $\left[\frac{\mathrm{I}}{\mathrm{HI}}\right]$ axis at the points +1, 0, and −1, corresponding to the condition that the strength of the acid HA is respectively less than, equal to, or greater than the strength of the indicator acid HI by one logarithmic unit (or to a factor of tenfold in the acid strength constants K_{HA}). Consequently for ideal solutes where the slope λ is unity, the intercept on either axis is a measure of the strength of the acid relative to the indicator.

(*b*) *Indicator or acid associated*

If either the indicator or the acid or both are associated, the simple relationship just developed will not hold. The deviations from the ideal mechanism could, of course, be taken care of by introducing activity coefficients, but it seems preferable to reformulate the mechanism in a way which will recognize the possibility of association, and thus diminish the burden which the activity coefficient must bear.

The stoichiometric concentration will be represented by brackets, and the activity by parentheses. The activity coefficient, *f*, will refer to any deviation from the behavior of an ideal solute, when the solute is considered as associated *m*-fold in the case of the acids, or *n*-fold in the case of the indicator.

The generalized mass law relations are:

$$a^{m}_{\mathrm{H}^+} = K'_{(\mathrm{HA})_m}\left[\frac{(\mathrm{HA})_m}{(\mathrm{A})_m}\right]\left(\frac{f_{(\mathrm{HA})_m}}{f_{(\mathrm{A})_m}}\right) \tag{7}$$

$$K_{(\mathrm{HA})_m}\left[\frac{(\mathrm{HA})_m}{(\mathrm{A})_n}\right] \tag{8}$$

$$a^{n}_{\mathrm{H}^+} = K_{(\mathrm{HI})_n}\left[\frac{(\mathrm{HI})_n}{(\mathrm{I})_n}\right] \tag{9}$$

It is important to note that K'_{HA} is an activity constant and consequently does not vary with change of solvent. The constant $K_{(\mathrm{HA})_m}$ in equation 8 is an acidity constant, i.e., equal to the activity constant times the activity coefficient ratio. The acidity constants will vary with changes in the medium and are the quantities which are actually employed. By extracting the m^{th} and n^{th} root, equating 8 and 9, and casting into logarithmic form, the general equation becomes:

$$\frac{1}{m}\log\left[\frac{(\mathrm{A})_m}{(\mathrm{HA})_m}\right] = \frac{1}{n}\log\left[\frac{(\mathrm{I})_n}{(\mathrm{HI})_n}\right] - \frac{1}{m}\,pK_{(\mathrm{HA})_m} + \frac{1}{n}\,pK_{(\mathrm{HI})_n} \tag{10}$$

Since m and n cannot be determined independently, multiply through by m and get the ratio $m/n = \lambda$. If, during the process of titrating an acid with a base B, no appreciable change in environment is produced, i.e., no change in activity coefficient ratio, then a plot of the color ratio log $\left[\frac{\text{I}}{\text{HI}}\right]$ against log $\left[\frac{\text{A}}{\text{HA}}\right]$ will yield a straight line, but with a slope λ. This actually proves to be the case. Interpreted physically, these equations mean that if λ is less than unity, one molecule of the associated indicator base can combine with more protons than can one molecule of the associated base A. In other words, a slope less than unity means that the indicator is associated relatively more than is the acid.

Figure 2 shows the results of titrating dichloroacetic, monochloroacetic, formic, benzoic, and acetic acids with diethylamine, using brom phenol blue as indicator. This figure is typical of the results obtained with other indicators. The slopes of the curves of these acids lie between one-third and one-half, depending upon the total concentration and the particular acid and indicator used. Most of the curves approximate most closely to a slope of 1/2, so that in general the degree of association of the indicator system is about twice that of the acid system.

Figure 3 gives the results for brom cresol purple, an indicator which in water changes in the acid range of pH 5.2 to 6.3 and thus is one logarithmic unit weaker than acetic acid. A similar relationship holds in benzene, except that acetic acid is only 0.3 logarithmic unit instead of one logarithmic unit more acid (i.e., higher) than brom cresol purple. In order to develop the basic color of brom cresol purple it is necessary to employ the strongest base which is soluble in benzene, namely, piperidine. In benzene, the piperidine–piperidinium system is only 1.4 *pK* units more basic or less acid than brom cresol purple, whereas in water the difference is 4.8 units. Saturation with water did not produce changes in relative acidity greater than 0.1 *pK* unit for monochloroacetic acid when compared with solutions which were especially dried and protected from moisture. This result is gratifying but the conclusion may have to be modified when very strong acids like hydrochloric acid are considered.

To determine the relative strengths of acids in respect to a given indicator, one has only to compare the intercepts on the log

$\left[\frac{A}{HA}\right]$ axes, i.e., at the point of half change of the indicator, for a numerical result. However, when the acid studied is more than one *pK* unit stronger or weaker than the indicator it becomes difficult to establish the intercept, since the equilibrium between acid and indicator systems is established so far from the point of half neutralization of the acid that a small experimental error becomes considerably magnified. This difficulty seriously restricts the number of acids that can be studied with a given indicator. However, if the relative acidity of two indicator systems

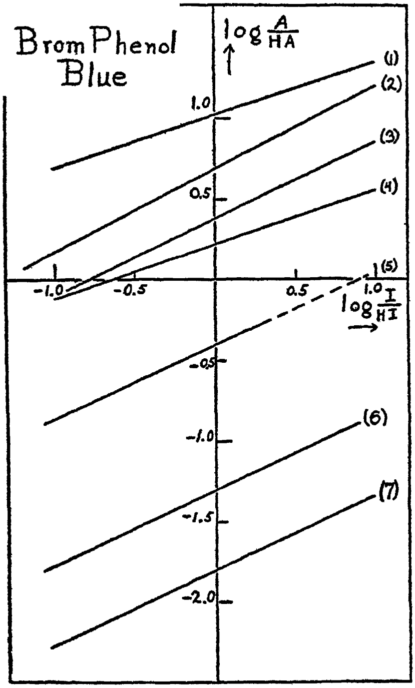

FIG. 2. BROM PHENOL BLUE

1.	Dichloroacetic acid	0 10 *M*
2.	Salicylic acid	0.01 *M*
3.	Monochloroacetic acid	0.01 *M*
4.	Monochloroacetic acid	0.10 *M*
5.	Formic acid	0.01 *M*
6.	Benzoic acid	0.01 *M*
7.	Acetic acid	0.10 *M*

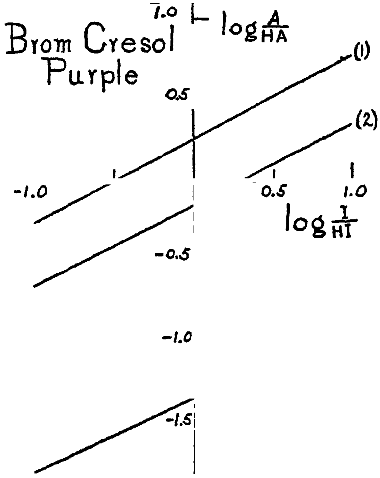

FIG. 3. BROM CRESOL PURPLE

1.	Acetic acid	0.1 *M*
2.	Diethylammonium ion	0.1 *M*
3.	Piperidinium ion	0.1 *M*

can be established, the acid systems studied with these two indicators can then be compared.

For example, dichloroacetic acid is weaker than dimethyl yellow but stronger than brom phenol blue. The experimental curves for these two indicators are then displaced along the log $\left[\frac{I}{HI}\right]$ axis until they become continuous. Dimethyl yellow is several units more acid than is brom phenol blue. By a progressive step-wise

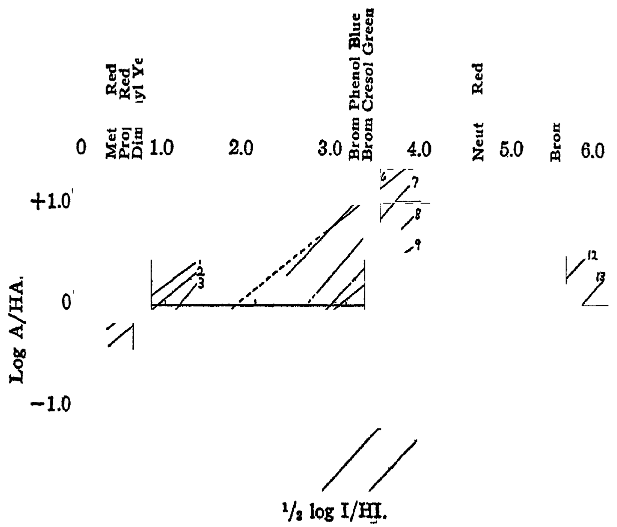

Fig. 4

1. Trichloroacetic acid.........	0.10 *M*	8. Monochloroacetic acid...	0.01 *M*
2. Trichloroacetic acid.........	0.05 *M*	9. Monochloroacetic acid...	0.10 *M*
3. Trichloroacetic acid........	0 01 *M*	10. Formic acid..............	0.01 *M*
4. Dichloroacetic acid.........	0 10 *M*	11. Benzoic acid..............	0.01 *M*
5. Dichloroacetic acid.........	0.05 *M*	12. Acetic acid...............	0.10 *M*
6. Dichloroacetic acid.........	0 01 *M*	13. Diethylammonium ion....	0.10 *M*
7. Salicylic acid...............	0.01 *M*	14. Piperidinium ion..........	0.10 *M*

correlation of the indicators in this manner, it is possible to establish a numerical scale for all the acid and indicator systems studied.

Figure 4 gives a summary of the results obtained by this procedure when plotted against 1/2 log $\frac{I}{HI}$ to compress the results into a reasonable space and also to make the results more comparable with the ideal case of unit slopes. The heavy lines represent the range over which experimental measurements can be made and the dotted lines the extrapolations employed in correlating the various indicator systems.

This figure provides a scale of acidity which is correct, within limits of experimental error, for those acids which are represented by lines having a unit slope and is approximately correct for those having slopes but slightly different from unity. This form of presentation has the advantage of representing the experimental results directly. Our knowledge of benzene solutions, however, is too incomplete at present to allow of a more exact interpretation of the effects of dilution.

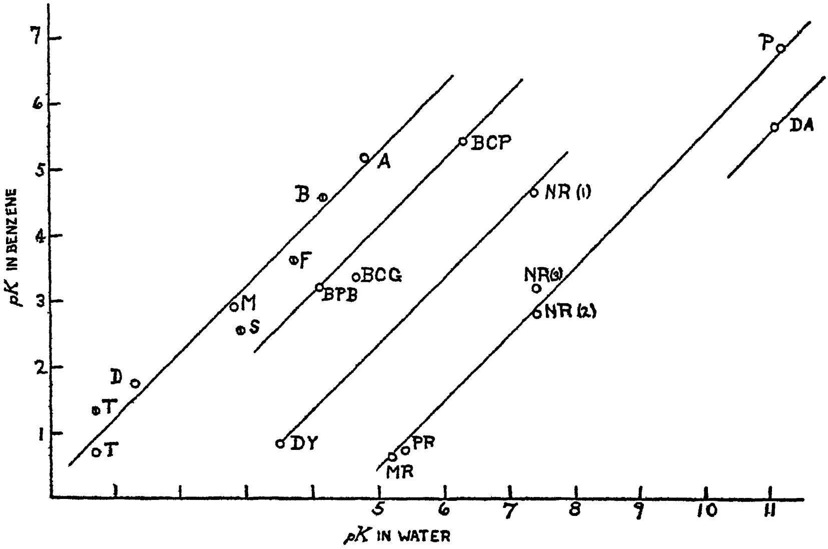

FIG. 5

T, Trichloroacetic acid..... 0.10 M
D, Dichloroacetic acid..... 0.10 M
M, Monochloroacetic acid.. 0.01 M
S, Salicylic acid........... 0.10 M
F, Formic acid............. 0.01 M
B, Benzoic acid............ 0.01 M
A, Acetic acid............. 0.10 M
BPB, Brom phenol blue
BCG, Brom cresol green

BCP, Brom cresol purple
DY, Dimethyl yellow
NR (1), Neutral red (1)
MR, Methyl red
PR, Propyl red
NR (2), Neutral red (2)
NR (3), Neutral red (3)
DA, Diethylamine
P, Piperidine

In figure 5, the acid strengths in water are compared with those in benzene by plotting the values of pK benzene obtained from the intercepts on $1/2 \log \frac{\text{I}}{\text{HI}}$ axis in the preceding figure. It is interesting and important to note that the uncharged acids retain practically the same differences in strength that exist in water. This means that their activity coefficient ratios undergo almost parallel changes when the acids are transferred from water to benzene. On the other hand, the strengths of the cationic acids represented by the indicators and substituted ammonium ions have increased to a very considerable amount over their strengths in water relative to the uncharged acids. It remains an interesting problem to determine whether these changes can be accounted for quantitatively on the basis of the electrical work of transfer, or whether it will be necessary to invoke further hypotheses dependent upon the molecular structure (10, 11). The answer to this question must await an independent determination of the charge type before definite conclusions can be drawn.

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THE QUANTITATIVE STUDY OF VERY WEAK BASES

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There are large groups of organic compounds for which basic properties have been demonstrated, but whose base strength is so small that its quantitative measurement is impossible within the limits of the classical field for the investigation of electrolytes, the dilute aqueous solution. Among these, the oxygen bases are of especial interest both in theory and in practice.

Thus the discovery by Collie and Tickle in 1899 of the salt-forming properties of the oxygen compound, dimethylpyrone, has led to a development by which the basicity of oxygen has become an important and recognized principle of organic chemistry (1). And the investigation by Hantzsch in 1908 (2, 3) of the properties of sulfuric acid as an electrolytic solvent demonstrated that nearly all oxygen compounds can act as bases provided only that the medium in which they are dissolved is of sufficiently high acidity. Yet quantitative progress has been so slow that only one determination of the base strength of an organic oxygen compound, that of dimethylpyrone by Walden in 1902 (4), had been published until very recently.

Such a discrepancy between qualitative and quantitative information is always distressing; it is particularly so in this case because of the important problems which wait upon the quantitative data. It is, for instance, a widely held hypothesis that catalysis by acids depends upon the addition of hydrogen ion to the substrate, which is to say upon basic properties in the substrate. In the light of Brönsted's relation between the catalytic effect of an acid or base and its strength (5), and of the evidence, presented at this meeting by myself and Pfluger, and to be published shortly, of a close relation between the strength of a carboxylic acid and the rate of addition of the corresponding methyl ester to a tertiary amine, a knowledge of the strength of acids and bases becomes of the greatest importance for the interpretation of reaction velocities. It seems indeed quite possible that the base strength of the substrate will be found to have an importance in an acid catalyzed reaction equal to that of the acid strength of the catalyst.

The first requirement for a quantitative study is a numerical definition of the quantity, base strength, in question. This necessitates some limitation of the field. In the ordinary parlance of organic chemistry a base is a substance like aniline, whose electrically neutral molecule is capable of adding a hydrogen ion to form a positive ion. This reaction it is convenient to call the ionization of the base. The extent of ionization increases with increasing acidity of the medium in which the base is placed, and with increasing strength of the base. Whether the ionization of a base, B, takes place by direct transfer of a hydrogen ion from an acidic substance

$$B + HA \rightleftarrows BH^+ + A', \text{ or,}$$
$$B + OH_3^+ \rightleftarrows BH^+ + H_2O$$

or whether it proceeds through intermediate steps to the same result, as has frequently been assumed,

$$B + H_2O \rightleftarrows BHOH$$
$$BHOH \rightleftarrows BH^+ + OH'$$
$$OH' + HA \rightleftarrows H_2O + A'$$

can have no significance for measurements which depend upon equilibrium states (6). The studies of Brönsted on catalysis by bases (5, 7) do however make the direct reaction much the more probable.

Cryoscopic and conductivity studies have shown that the typical organic acids, esters, ketones, aldehydes, and ethers, as well as the amines and amides, act as bases in this sense when they are dissolved in 100 per cent sulfuric acid (2, 3). Such substances I have referred to as simple bases (8). For hydroxy compounds direct evidence of a simple basic ionization is lacking, because these give much larger freezing point depressions in sulfuric acid than do simple monoacid bases. Hantzsch's interpretation (2) is the reaction

$$(C_6H_5)_3COH + 2H_2SO_4 \rightleftarrows (C_6H_5)_3C^+ + OH_3^+ + 2HSO_4'$$

in the case of triphenylcarbinol derivatives, and

$$CH_3OH + 2H_2SO_4 \rightleftarrows CH_3OSO_2OH + OH_3^+ + HSO_4'$$

in the case of simple aliphatic alcohols. The available evidence is, however, hardly sufficient to justify the assignment of different ionization mechanisms and osmotic factors to the two groups of substances. α,β-Unsaturated ketones containing more than one ethylene group have a similarly complex ionization in sulfuric acid (9, 3). It is clear that the strengths of these pseudo bases measured by complex ionization reactions are incommensurable with those of simple bases.

If, moreover, following Brönsted (10) and Lowry (11) we extend the definition of the word "base" to include all molecules and ions which can add a hydrogen ion, we find that the relative strength of two bases, one neutral and the other charged, say aniline and acetate ion, is greatly affected by a change in medium, whereas the relative strength of two bases of the same electrical type is not (12, 13).

The base strength discussed in what follows pertains therefore exclusively to simple, electrically neutral, monoacid bases. For its quantitative measurement we must ultimately depend in every case upon the determination of concentrations. In particular the only experimental measure of the relative strength of two bases, B and C, is the position of equilibrium in the reaction

$$B + CH^+ \rightleftarrows BH^+ + C$$

which is to say, the value of the concentration ratio

$$\frac{C_B \cdot C_{CH^+}}{C_{BH^+} \cdot C_C}$$

So long as we remain within a medium of constant properties so that the law of equilibrium in terms of concentrations is applicable, the relative strength of two bases, B and D, follows directly if the relative strengths of the pairs, B and C, and C and D, are known. Since, further, we measure only relative strengths, we shall have to fix arbitrarily the strength of some one base in order to obtain a numerical scale.

All this gives measures of relative strength only for one particular medium, that in which the comparison is made. The crucial question for the present inquiry is whether these will also be valid measures for other media; for instance, whether the relative strength of two very weak bases in glacial acetic acid or in a 75 per cent sulfuric acid–water mixture is the same as it is in water, in which the ionization is too small for direct measurement. To this no complete answer can yet be given. The rule that the relative strengths of a series of bases of the same electrical type are independent of the medium is certainly a valuable first approximation. As such its validity has been amply demonstrated (14), even for so extreme a case as that represented by a transfer from water to benzene as a solvent (15). As an exact rule, it has been found applicable within the precision of the most careful colorimetric measurements for certain ranges of medium variation. This will be referred to later in this paper. Beyond this its limits of precision and range are not definitely established and require demonstration in every case of its application (40).

The rule may be given a certain theoretical background in terms of considerations first suggested by Bjerrum and Larsson (16). The quantity

$$K' = \frac{a_{\mathrm{B}}\, a_{\mathrm{H}^+}}{a_{\mathrm{BH}^+}}$$

where the a's are activities (referred for all media to one common standard of reference rather than to infinite dilution in each solvent), is a universally valid but not directly determinable inverse measure of the strength of the base B. The concentration equilibrium ratio for two bases is related to these constants by the equation

$$\frac{C_{\mathrm{B}} C_{\mathrm{CH}^+}}{C_{\mathrm{BH}^+} C_{\mathrm{C}}} = \frac{K'_{\mathrm{B}}}{K'_{\mathrm{C}}} \times \frac{f_{\mathrm{BH}^+} f_{\mathrm{C}}}{f_{\mathrm{B}} f_{\mathrm{CH}^+}}$$

where the f's are activity coefficients. Only to the extent that the f ratio in this equation is constant will the relative strength of the two bases be independent of medium variations. Each f, being a measure of the deviation of the solute from ideality, is a function of the energy of interaction of the molecules of the solute with those of the medium. For the ion of an organic base, which is a large molecle bearing a localized charge and quite different from the spherically symmetrical ion of the Debye-Hückel theory, this interaction energy is the sum of two terms of coördinate importance and relative independence, one representing the energy due to the charge, the other that due to the rest of the molecule. Because of the logarithmic relation between the activity coefficient and the energy, we may therefore write

$$f_{BH^+} = f^e_{BH^+} f^u_{BH^+}$$

where $f^e_{BH^+}$ is a function of charge and of what may be called the effective diameter of the atom bearing the charge, but not of any other properties of the ion; and $f^u_{BH^+}$ is a function of dipole interactions and van der Waals forces which are of nearly the same magnitude in the ion as in the neutral base (17). We may therefore set

$$f^u_{BH^+} = f_B,\ f^u_{CH^+} = f_C$$

and

$$\frac{C_B C_{CH^+}}{C_{BH^+} C_C} = \frac{K'_B}{K'_C} \times \frac{f^e_{BH^+}}{f^e_{CH^+}}$$

The ratio $f^e_{BH^+}/f^e_{CH^+}$ should be very nearly one for organic bases, since the charge is the same and the diameter of the oxygen or nitrogen atom carrying the charge is nearly the same for the two bases.

The first advance in the direction of the use of media of acidity higher than is attainable in dilute aqueous solutions was made by Conant and Hall (18) with acetic acid as a solvent. Electrometric, indicator, and catalytic studies were made in this solvent, and the whole scale was found to be shifted toward the acid side when compared with aqueous solutions. The important observation was made that the relative strengths of those bases which can be measured both in the aqueous and in the acetic acid systems is unaltered by the shift from the one to the other within the precision of the measurements. The extrapolation of the rule that there is no shift to bases which cannot be directly measured in both media is therefore a safe one. Among the very weak bases thus studied anisalacetophenone (19) and a group of triphenylcarbinols (20) are especially notable.

This most important step still does not carry us far enough toward the acid side for a general attack on the base strength of oxygen compounds. The obvious extension to the use of stronger acids is important and desirable, although its utility for the present purpose is likely to be limited. Thus formic acid is a more acid solvent than acetic acid, but it is also relatively basic (21, 22). The resultant large solvent ionization masks the ionization of the weaker bases, and severely restricts the range of base strengths accessible to investigation in it. As for inert solvents, which are very weakly basic without being strongly acidic, these are rarely if ever satisfactory solvents for electrolytes. This is not merely an inconvenience but a difficulty in principle. The more widely we depart for the measurement of base strengths from the hydroxylic, good salt solvent, high dielectric constant type of solvent in which the most important applications are likely to be made, the greater becomes the danger of error due to a shift in relative base strength.

A medium whose acidity varies continuously from that of water to that of sulfuric acid and which is liable to no such objections is obtained by mixing the two liquids in varying proportions. Against these advantages we must set one real and one apparent disadvantage. The apparent disadvantage is the fact that these solutions are neither ideal nor dilute. We find, however, that no shift in relative strength of a series of bases results from those changes in medium properties which accompany the variation of the proportion of acid and water. The apparent disadvantage translates itself therefore into an opening out of this field of concentrated solutions to quantitative investigation, not only for the determination of base strength, but for reaction velocity and solubility studies. The real disadvantage is the fact that the mixtures are so heavily buffered that no reasonable addition of base can change significantly any property of the solution as a whole. We cannot therefore rely upon a measurement of the conductivity or acidity of the solution but must use some specific property of the base, recognizable and measurable in the mixture, and altered by conversion of base to ion in a recognizable and measurable fashion.

One such property is that of light absorption. The loss or gain of a hydrogen ion by an organic acid or base, its ionization, seems to be accompanied by a change in light absorption in every case in which there is absorption at all (23). When the neutral molecule or the ion is colored, this results in appearance or disappearance of color when ionization takes place or in a large change in color quality or intensity. When the absorption is in the ultraviolet the fact is less obvious but apparently just as general (24 to 31). Whether or not the reason for the difference in color between neutral molecule and ion is a change in structure capable of representation by our usual symbols is unimportant for the present purpose so long as the difference exists. Even if molecule or ion is present as a mixture of tautomers in mobile equilibrium, the color is still a valid measure of degree of ionization, as was long ago demonstrated by A. A. Noyes (32). In so far as acids are concerned, it is now well-established that no tautomeric equilibrium is concerned in the ionization and that the acid may be represented by one single structural formula, the ion by another (33, 34).

The first attempt to base some sort of a quantitative measure of the strength of very weak bases upon the difference in color between base and ion was that of Baeyer and Villiger in 1902 (35). They dissolved the base in a mixture of acetic and sulfuric acids, and measured its strength by the volume of 75 per cent aqueous ethyl alcohol required to destroy the color of the solution. The same method and closely similar ones (36) have been much used, more largely however for pseudo bases of the triphenylcarbinol and dibenzalacetone types than for simple bases. Ziegler and Boye (37) found however that very serious error may arise from the fact that the amount of basic solvent required for decolorization is just as much a function of the color intensity of the ionized form as it is of the base strength. They suggest the measurement of base strength by the quantity of basic solvent required to reduce the color intensity not to zero but to a definite fraction of that possessed by the completely ionized substance. This certainly rates the bases in the proper order, but does not lead to the quantitative measure of base strength as it has here been defined.

With the development of precise methods for the colorimetric study of indicators, it has become possible to determine the relative strength of two simple bases which possess indicator properties and are not too widely separated in strength by the colorimetric determination of the degrees of ionization of both in a suitable acid–water mixture (8). There are some complications arising from the fact that ionization is a sufficient but not a necessary condition for color change, and the results have to be corrected for the change in light absorption due to the change in the nature of the medium necessary to obtain the reference colors of base and ion. The correction seems to be quite satisfactory in most cases and the overall precision of the comparison is about ±4 per cent.

By this method a number of nitrogen and oxygen bases ranging in strength from *p*-nitroaniline, which is appreciably ionized in water, to trinitroaniline, which is incompletely ionized in sulfuric acid, have been studied by myself and Deyrup (8) with the result that constancy of relative strength has been thoroughly verified. That is, it was found that the relative strength of any two bases is the same for the whole range of sulfuric acid–water mixtures in which they can be directly compared. It was likewise found to be the same for mixtures of perchloric acid and water and for solutions in anhydrous formic acid. Unpublished work by myself and Paul shows that the same values are obtained for a number of these indicators in mixtures of hydrochloric and of nitric acids with water.

It is impossible by this or any other method to compare directly the strengths of two bases when these differ so widely that the ionization of the one becomes appreciable only in media of acidity so high that the ionization of the other is practically complete. Such bases may however be compared by an indirect or step method which uses a series of bases intermediate in strength between the two extremes to be compared and sufficient in number to make possible direct comparison between successive members of the series. In this way numerical values were obtained for all of the bases studied, using the strength of *p*-nitroaniline in aqueous solution as a natural reference point. The determination of the strength of any simple monoacid base which has indicator or halochromic properties by comparison with this series has therefore become a simple matter.

Where no visible color change accompanies the ionization, some other criterion must be found for the determination of the ionization ratio. One possibility which is now being investigated at Columbia University uses the change in ultra-violet absorption which accompanies ionization; in effect it extends the colorimetric method from the visible to the ultra-violet.

Among the other optical methods which suggest themselves is one of limited applicability for which some data is already available. Baker (38) has shown that the large change in rotation observed when camphor is dissolved in sulfuric acid is at least partly the result of salt formation.

A method of quite a different sort depends upon the behavior of the solubility of organic oxygen compounds in mixtures of strong acids with water. In unpublished work in this laboratory Deyrup found that this increases very sharply within a narrow range of acid concentration and in a way which strongly suggests that conversion of the base to the ion in the range of acidities there attained is responsible for the increase in solubility. Quantitative studies by Dr. Chapman show that in many instances the course of the increase agrees with this assumption, and that solubility measurements in sulfuric acid–water mixtures may be used for the determination of base strength.

Equivalent in principle to the determination of base strength by solubility is its determination by distribution. The possibility of measuring the distribution of organic compounds between sulfuric acid–water mixtures and ligroin has been demonstrated by Baker and his coworkers (39), and the method has been used by them for the qualitative study of the basicity of benzaldehyde, acetophenone, ethyl benzoate, and other oxygen compounds. It should be especially valuable with bases whose solubility as neutral molecules is large in the acid–water mixtures, or where the appearance of new phases, bisulfates of the organic base, complicate the solubility method.

SUMMARY

It is shown that several methods are available for the translation of the existing qualitative knowledge that the typical organic ketone, aldehyde, ester, acid, or ether is a base into a quantitative knowledge of its basic strength.

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THEORIES OF CONCENTRATED ELECTROLYTES

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The kinetic theory of electrolytes aims to account quantitatively for the thermodynamic and other properties of electrolytic solutions from reasonable assumptions about the forces between the ions. The approximate theory developed by Debye and Hückel for the effects of Coulomb forces is generally recognized as sound, and the consequent theoretical limiting laws for low concentrations of ions have been amply verified by experiments. For the extension of this theory to concentrated solutions, more accurate computations of the Coulomb forces are needed; in addition, it becomes necessary to make more specific assumptions about the non-Coulomb forces, which are important for small distances between the ions. This theory of concentrated electrolytes has met with many difficulties; in part, conflicting results have been deduced.

GENERAL STATISTICAL METHODS

Before we examine the different contributions to the field, we shall review briefly some of the common methods for computing thermodynamic functions from molecular mechanical models, and show the connection with the fundamental principles of statistical mechanics.

The "adiabate principle," which will be our main tool, takes its simplest form for a thermally isolated system, namely, the following relation between the energy E and the "reversible work" δW:

$$\delta E = \delta W = -\overline{K}\,\delta a = \overline{\partial E/\partial a}\,\delta a \tag{1}$$

where δa denotes the change of any parameter a (e.g., volume, molecular size, electric charge, etc.), and the average of the corresponding force K is taken over all phases of the molecular motion.

If a system is not thermally isolated but, instead, is kept at a constant temperature T, we must replace E by the "free energy"

$$F = E - TS$$

where S is the entropy, now variable, and the relation given by 1 is replaced by

$$\delta F = \delta W = -\overline{K}\,\delta a = \overline{\partial E/\partial a}\,\delta a \tag{2}$$

For averages taken at a given temperature T, it is legitimate to employ the "canonical ensemble" of Gibbs. The "phase-space" Ω

$$d\Omega = dq_1\,dq_2 \ldots dq_f\,dp_1\,dp_2 \ldots dp_f$$

(q = coördinate, p = impulse) is occupied with the local density

$$\exp\left((F - \epsilon)/kT\right) \tag{3}$$

where the energy ϵ is now a function of the coördinates and impulses:

$$\epsilon = \epsilon\,(q_1, \ldots q_f;\ p_1, \ldots p_f)$$

This function determines the mechanical properties of the system. The free energy F itself is determined directly by the condition

$$\int \exp\left((F - \epsilon)/kT\right) d\Omega = 1 \tag{4}$$

As a rule, certain conventional factors involving numbers of particles, Planck's constant, etc., are added to equation 4; these will be constant throughout our considerations and so need not concern us.

For a given temperature T, we want to know how F depends on parameters a_1, a_2, ... ,which enter into the function

$$\epsilon = \epsilon(q_1, \ldots q_f;\ p_1, \ldots p_f;\ a_1, a_2, \ldots)$$

According to equation 4, for constant T,

$$\int [\delta F - \delta\epsilon] \exp\left((F - \epsilon)/kT\right) d\Omega = 0$$

$$\delta F = \int \left[\frac{\partial\epsilon}{\partial a_1}\,\delta a_1 + \frac{\partial\epsilon}{\partial a_2}\,\delta a_2 + \ldots\right] \exp\left((F-\epsilon)/kT\right) d\Omega = -\overline{K_1}\,\delta a_1 - \overline{K_2}\,\delta a_2 - \ldots$$

which amounts to a verification of the formula 4 for F in terms of the canonical distribution ("phase integral"). However, besides verifying the statistical representation of macroscopic reversible work, our derivation also shows that, if the general premises of the statistical theory are correct, similar reasoning may be applied with equal confidence to the purely fictitious operation of changing any molecular parameter.

The canonical distribution is a generalization of the Maxwell-Boltzmann distribution law to the entire phase-space. We shall show next how the Maxwell-Boltzmann formula can be generalized, for a reduced number of degrees of freedom, to the case of fluctuating forces. That is, we consider a subspace, for example dq_1, of the entire phase-space

$$d\Omega = dq_1\, d\Omega'$$

(we may of course equally well take out several factors: dq_1, dq_2, ... of $d\Omega$), and we want to compute the probability for finding q_1 in the range $q_1' < q_1 < q_1' + \Delta\, q_1$. This probability we denote by

$$f(q_1')\, \Delta q_1 = \exp(-\, w(q_1')/kT)\, \Delta q_1$$

and according to equation 3,

$$f(q_1) = \int \exp\,((F - \epsilon)/kT)\, d\Omega' = \exp\,(-\, w(q_1)/kT) \tag{6}$$

where now

$$\int \exp\,(\,(F + w(q_1) - \epsilon(q, p, a)\,)/kT)\, d\Omega' = 1 \tag{7}$$

In these integrations, q_1 is kept constant, otherwise every formula is analogous to the case of the entire phase integral. In effect, we are now treating q_1 like a parameter (a); the advantage of this treatment is that the analog of equation 5 still holds. As before

$$\frac{\partial}{\partial a}(F + w(q_1)\,) = \overline{\partial\epsilon/\partial a}' \tag{8}$$

for any parameter a, while as regards q_1 itself, it does not enter into F, so that

$$\partial w/\partial q_1 = \partial(F + w(q_1)\,)/\partial q_1 = \overline{\partial\epsilon/\partial q_1}' \tag{9}$$

Here we have shown that the potential $w(q_1)$, which (for the case of fluctuating forces) replaces the energy in the Maxwell-Boltzmann distribution, is *the potential of the average force.* This result was used by Einstein and Smoluchowski in the theory of fluctuations.

At times it may be convenient to consider some of the parameters a as variables in the computation of $w(q_1)$. The procedure is straightforward: Since F depends only on a, we have

$$w(q_1'',a') - w(q_1',a') = [F(a') + w(q_1'',a')] - [F(a') + w(q_1',a')] =$$

$$= \int_{(q_1',\, a')}^{(q_1'',\, a')} [\,(\overline{\partial\epsilon/\partial a})\, \delta a + (\overline{\partial\epsilon/\partial q_1})\, \delta q_1] \tag{10}$$

THE COMPUTATION OF THE COULOMB ENERGY

By the methods outlined in the preceding section, it is fundamentally possible to calculate the deviations from the laws of ideal solutions whenever adequate information about the forces between the *solute* molecules is available. Certain rather trivial distinctions between the "free energies" at constant pressure *viz.* volume etc. should be observed; the complications in question, which recur everywhere in the kinetic theory of real solutions, are more tedious than important, and we shall content ourselves here with a reference to Bjerrum's discussion (1) of the corresponding thermodynamic distinctions.

The electrostatic contribution to the free energy of an electrolyte can be computed if the average potential $\psi^*(\eta)$ due to other ions at the point of an ion of charge η is known (as a function of η and of the composition of the solution), because then, on the basis of the preceding general considerations,

$$F_{el} = \sum_{i=1}^{N} \int_{\eta=0}^{\eta=e_i} \psi^*(\eta)\, d\eta \tag{11}$$

where the sum is extended over all the ions present. The function $\psi^*(\eta)$ depends on the instantaneous composition of the solution, which changes during the charging process, and on the momentary charge η of a selected ion. The ions may be charged simultaneously or one at a time, in arbitrary sequence; the result should be independent of any such choice of the charging process, provided that the functions $\psi^*(\eta)$ are correct, or at least consistent. It was pointed out by Güntelberg (2) that the work of charging one ion in a given solution yields directly the electrostatic contribution to the thermodynamic potential (partial free energy) of that ion:

$$\mu_{i\mathrm{el}} = \partial F_{\mathrm{el}}/\partial N_i \int_0^{e_i} \psi^*(\eta)\, d\eta \tag{12}$$

The derivation from equation 11 is obvious. Only one precaution must be observed in using either equation 11 or 12: The electrostatic free energy F_{el} may not represent the entire deviation from the laws of ideal solutions, because non-Coulomb forces may also cause a contribution to F (and to μ_i).

The main problem in the theory of strong electrolytes is the calculation of $\psi^*(\eta)$. Debye and Hückel (3) worked out the first successful method of attack, and up to the present no fundamental improvement has been introduced. They assume that the average concentration $n_{ji}(r)$ of ions of the species i at a distance r from a given ion of the kind j is related to the mean potential $\psi_j(r)$ at this distance from the j ion by Boltzmann's equation

$$n_{ji}(r) = n_i \exp(-e_i\psi_j/kT) \tag{13}$$

and with the aid of Poisson's equation

$$\mathrm{div\ grad}\ \psi_j = -\frac{4\pi}{D}\sum_i n_{ji}e_i \tag{14}$$

obtain an equation for ψ_j alone

$$\mathrm{div\ grad}\ \psi_j = -\frac{4\pi}{D}\sum_i n_i e_i \exp(-e_i\psi_j/kT) \tag{15}$$

This "Poisson-Boltzmann" equation was not solved completely by Debye and Hückel; they were content with the approximation

$$\exp(-e_i\psi_j/kT) \sim 1 - (e_i\psi_j/kT) \tag{16}$$

which leads to the approximate equation

$$\text{div grad } \psi_j = \kappa^2\psi_j \tag{17}$$

$$\kappa^2 = \frac{4\pi}{DkT}\sum_i n_i e_i^2$$

and its solution

$$\psi_j = \frac{e_j}{D(1 + \kappa a)} \frac{\exp\ (\kappa(a - r))}{r} \tag{18}$$

where a denotes the least distance of approach of (any) two ions. The potential of interaction becomes proportional to the charge:

$$\psi^*(\eta) = - \kappa\eta/D(1 + \kappa a) \tag{19}$$

The approximation of formula 16 is poor for small distances r (because $\psi \sim 1/r$), and the efforts of later workers have largely been directed towards the elimination of this error.

Partly for this purpose, and partly in order to consider strong and weak electrolytes from a common point of view, Bjerrum (4) improved formula 16 by separate consideration of the cases where two ions (of opposite charges) come closer than a certain distance q:

$$q = - e_j e_i/2DkT > a > 0$$

Such couples of ions Bjerrum treats as undissociated molecules, *viz.*, particles of charge $(e_j + e_i)$, and he corrects the concentrations n_1, n_2, ... of "free" ions accordingly. For distances $r > q$, he retains the approximate equation 17, with k given by the corrected ion concentrations. In terms of Gibbs' phase integral (formula 4), one may say that Bjerrum applies different approximations to different regions of the space in evaluating the integral. Bjerrum was able to represent a more extensive range of experimental data than was possible with equation 19 as used by Debye and Hückel. For example, in order to describe the behavior of certain (relatively weak) electrolytes by equation 19, impossible values of a (<0) are required; but the adaptation of Bjerrum's theory leads to reasonable ionic diameters a.

H. Müller (7, 8) and Gronwall, La Mer, and Sandved (9) under-took the task that neither Debye and Hückel nor Bjerrum had attempted, of solving the complete Poisson-Boltzmann equation, after Gronwall (5) and La Mer and Mason (6) had made some advances in this direction. Recently, the computations for asymmetrical electrolytes have been completed by La Mer, Gronwall, and Greiff (10). Numerical integration or some method of successive approximation must be used; the preference is merely a matter of convenience.

While all these computations are based on the same equation and each one is sound, nevertheless one point of controversy remains. H. Müller computed the thermodynamic functions from the potentials by the easiest method, that is the Güntelberg principle, equation 12. Gronwall, La Mer, and Sandved (9) preferred the charging process used by Debye and Hückel, and pointed out that the Güntelberg method leads to somewhat different results; thereupon Müller (8) accepted their criticism and estimated his own "error," which turned out to be fairly small.

In view of the general results derived in section I, we must take a different view of Müller's "error," namely that either charging process is legitimate, but the Poisson-Boltzmann equation 15 is not entirely self-consistent. The requirement of consistency implied by equation 11 is that

$$\psi^*(e_1)\,\delta e_1 + \psi^*(e_2)\,\delta e_2 + \ldots + \psi^*(e_N)\,\delta e_N = \sum_i n_i\psi^*(e_i)\,\delta e_i = \delta F_{el}$$

should be a total differential, which involves reciprocal relations of the type

$$n_1\,\partial\psi^*(e_1)/\partial e_2 = n_2\,\partial\psi^*(e_2)/\partial e_1 \tag{20}$$

(The actual differential quotients and relations are complicated by the restriction $\Sigma n_i e_i = 0$, but only in a trivial fashion.)

The Poisson-Boltzmann equation 15 is not exact, because the underlying equation 13 is only an approximation. According to equations 6 and 9, we know that

$$n_{ji}(r) = n_i \exp(-w_{ji}(r)/kT) \tag{21}$$

where $w_{ji}(r)$ denotes the work expended (against the average force) in bringing two ions i and j from infinity to the distance r. Incidentally, we note that whenever a j ion is at the distance r from an ion of the kind i, then *vice versa,* whence

$$n_j n_{ji}(r) = n_i n_{ij}(r)$$

and, as one might expect

$$w_{ji}(r) = w_{ij}(r) \tag{22}$$

Equation 13, the fundamental assumption involved in the Poisson-Boltzmann equation, is obtained from equation 21 above by the approximation

$$w_{ji}(r) \sim e_i \psi_j(r) \tag{23}$$

applied to the "atmosphere" of the j ion in computing $\psi_j(r)$, while $\psi_i(r)$ is computed from the assumption.

$$w_{ji}(r) \sim e_j \psi_i(r) \tag{24}$$

We have to expect

$$e_i \psi_j(r) \neq e_j \psi_i(\mathrm{r}) \tag{25}$$

except in very symmetrical cases. Therefore we have found here, deep in the foundations of the theory, a discrepancy that reminds one quite strikingly of the discrepancy between different charging processes, when the condition for consistency of the latter is expressed by equation 20.

The approximate character of the Poisson-Boltzmann equation was recognized by Fowler (11) and by myself (12) some time before the question about the Güntelberg principle was raised. While my own reasoning was substantially that outlined above, Fowler (11) followed a different line of attack, and derived certain corrections to equation 15, which he expressed by the fluctuations of the forces on the ions, but did not actually compute. It will be shown in the Appendix to this article, that Fowler's "fluctuation-terms" are of the same order of magnitude as the maximum of the main terms in equation 15, but they are nearly cancelled (at least in some significant cases) by a supplementary term, which he omitted through an oversight. Since I do not see any way to exploit Fowler's method, I shall refer the reader to the Appendix for details.

The formulas 23 and 24 would hold exactly[1] if the mean distribution of charge in the neighborhood of a pair of ions i and j, at a distance r from each other, were always the sum of the charges induced by the two ions separately; because then the average force acting on either ion in the given configuration would correspond to the average electric field at the distance r from the other,—the force from its own atmosphere vanishes due to symmetry. This could not be true unless

$$\psi_1/e_1 = \psi_2/e_2 = \dots \tag{26}$$

for all the ions in the solution, considering that both the formulas 23 and 24 must be valid. For low concentrations, small charges, and large ionic diameters, equation 26 is indeed very nearly fulfilled; the approximate formula 18 conforms exactly to this condition. However, as soon as the higher terms in the Poisson-Boltzmann equation become important, we can no longer expect the ionic atmospheres to be additive, and then the Poisson-Boltzmann equation itself becomes unreliable.

Unfortunately, it is a very complicated task to improve this equation. I shall render here, in more definite form than before, a suggestion made by Fuoss and myself (13), which seems sound, although it would involve much tedious labor. We consider a more general distribution-function than that of equation 13, namely

$$\begin{aligned} f_{i_1, i_2, \dots, i_\nu}(P_1, P_2, \dots, P_\nu) = \\ = n_{i_1} n_{i_2} \dots n_{i_\nu} \varphi_\nu(P_1, e_{i_1}; P_2, e_{i_2}; \dots; P_\nu, e_{i_\nu}) \end{aligned} \tag{27}$$

so defined that

$$f_{i_1, i_2, \dots, i_\nu} \, dV_1 \, dV_2 \dots dV_\nu$$

equals the probability for finding ions of the species i_1, i_2, . . ., i_ν, (some of which may be identical) in volume elements dV_1,

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[1] Except for a slight modification due to short range forces (*v. i.*).

$dV_2, \ldots, dV_\nu$ surrounding the points $P_1, P_2, \ldots, P_\nu$, respectively. Moreover, let the electric field due to these ions in these positions, together with the charges which they induce in their environment possess at the point P an average potential

$$\psi_{i_1, i_2, \ldots, i_\nu}(P_1, P_2, \ldots, P_\nu; P) = \\ = \xi_\nu(P_1, e_{i_1}; P_2, e_{i_2}; \ldots; P_\nu, e_{i_\nu}; P) \tag{28}$$

For simplicity, we assume that all the ions have the same diameter a, so that the functions f and ψ (which always refer to a given electrolyte) depend only on the points $P_1, \ldots P_\nu$ and on the charges $e_{i_1}, \ldots, e_{i_\nu}$, as indicated by the equations 27 and 28. We now focus our attention upon the functions φ_ν and ξ_ν and let these functions be defined, not only for all configurations $(P_1, \ldots, P_\nu)$, but also for any set of charges $(\eta_i, \ldots, \eta_\nu)$, whether the concentrations of ions with these particular charges be finite or zero. The Poisson equation takes the form

$$\text{div grad } \xi_\nu(P_1, \eta_1; P_2, \eta_2; \ldots; P_\nu, \eta_\nu) = \\ = -\frac{4\pi}{D}\sum_i n_i e_i \frac{\varphi_{\nu+1}(P_1, \eta_1; P_2, \eta_2; \ldots; P_\nu, \eta_\nu; P, e_i)}{\varphi_\nu(P_1, \eta_1; P_2, \eta_2; \ldots; P_\nu, \eta_\nu)} \tag{29}$$

The main difficulty is to find a suitable generalization of the Boltzmann equation. For this purpose, we adapt our equation 10 as follows: The change of φ_ν due to a change of, say, the charge η_k of the ion at the point P_k, can be computed from the work expended in discharging that ion at some point far away from $P_1, \ldots, P_\nu$, and recharging it at the point P_k. This consideration leads to

$$-kT\frac{\partial}{\partial \eta_k}\log \varphi_\nu(P_1, \eta_1; \ldots; P_k, \eta_k; \ldots; P_\nu, \eta_\nu) = \\ = \partial w/\partial \eta_k = \lim_{P=P_k}\left(\xi_\nu(P_1, \eta_1; \ldots; P_k, \eta_k; \ldots; P_\nu, \eta_\nu; P) - \xi_1(P_k, \eta_k; P)\right) \tag{30}$$

where the definition by a limiting process is necessary on account of the self-potential η_k/Dr of the ion. The integration-constant in equation 30 will be nearly equal to

$$\prod_{i,k}(1 - \delta(P_i, P_k)) \sim \varphi_\nu(P_1, 0; P_2, 0; \ldots; P_\nu, 0) \tag{31}$$

where

$$\delta(P_i, P_k) = \begin{cases} 1, \text{ for } r_{ik} < a \\ 0, \text{ for } r_{ik} > a \end{cases} \tag{32}$$

but on account of deviations from random arrangement due to Coulomb forces as well as short range repulsion (expressed by the diameter a), equation 31 will only be an approximation, although probably a good one. We shall leave this question aside, and return to the system formed by the equations 29, 30, 31. As it stands, this system is not determinate, but suppose that we expand φ_ν and ξ_ν in power series of $\eta_1, \eta_2, \ldots, \eta_\nu$, whereby the coefficients will be functions of the configuration $(P_1, P_2, \ldots, P_\nu)$. Next, in ξ_ν we neglect all powers of order higher than ν (in all the charges $\eta_1, \eta_2, \ldots, \eta_\nu$ together); then $\xi_{\nu+1}$ will contain only the same types of terms that are already contained in ξ_ν, and the difference between the coefficients of corresponding powers in ξ_ν and in $\xi_{\nu+1}$ will probably be small. If we may neglect this difference, we can obtain a determinate system of equations. However, it remains to investigate how the power series for the functions φ_ν should be abbreviated, if at all, in order to obtain good approximations and consistent results; (the integral of the differential equation 30 should be independent of the path of integration). Also, it seems likely that the approximation expressed by formula 31 will give rise to similar questions. These problems have not been analyzed, and I do not expect to take them up in the near future. Incidentally, the above scheme for abbreviating the power series expansions of φ_ν and ξ_ν may not be the most suitable.

I have made a few tentative computations of the corrections to be applied to equation 15, by the method outlined here. These computations indicate that as long as the difference between equation 15 and the approximate equation 17 may be regarded as a correction to the latter, *the corrections to equation 15 are of a higher order*, involving higher powers of the concentrations as well as the charges. In such cases the Poisson-Boltzmann equation 15 is probably a very good approximation.

It is worth pointing out that Bjerrum's method of computation takes into account the reduction of the effective ion concentration due to pair-wise association, perhaps the most important among the effects that are neglected by the Poisson-Boltzmann approximation. Therefore, while one may expect that the latter will be the more accurate for relatively strong electrolytes, it seems probable that Bjerrum's method will give better results in cases where the majority of the ions are present in the form of neutral pairs (corresponding to higher powers in the expansion of the Boltzmann formula).

SHORT RANGE FORCES

The fact that the electrostatic energy of the ions is finite proves that repulsive forces are superimposed on the Coulomb forces for molecular distances. So far, we have represented these repulsive forces by a minimum distance of approach, the "diameter" *a*, and we have considered their effects only to the extent that they limit the electrostatic energy. Now, whether there are Coulomb forces (ions) or not (molecules), repulsive forces will cause a direct contribution of their own to the free energy of any system. Incidentally, we have reasons to believe that the repulsive forces between the molecules decrease quite rapidly with the distance, even faster than the forces of ordinary cohesion. If so, then these forces can be represented for most purposes by a large discontinuity of the potential energy at some distance $r = a$, and the corresponding contribution to the free energy can be computed in terms of the excluded volume, per particle

$$\Delta\mu_s = kT\,(\Sigma\,\frac{4\pi}{3}\,a^3/V) \tag{33}$$

where V is the total volume of the system. Van der Waals (14) derived the equivalent of this formula while dealing with intermolecular forces in gases (the well-known "*b*" in his equation). Boltzmann and others computed certain corrections due to the overlapping of "excluded spheres," but we shall not enter into such refinements.

The activity coefficients exp $(\Delta\mu\ kT)$ of the strongest electrolytes in water increase for high concentrations and exceed unity, which means that the effect of the repulsive forces, as expressed by formula 33, outweighs that of the Coulomb attraction. The magnitude of the effect requires appreciably greater diameters a for the ions in solutions than in crystals; the difference must of course be ascribed to the attraction between the ions and the solvent. The a values derived from formula 33 need not agree exactly with those that are used in computing the Coulomb energy, because the picture of "hard billiard balls" is certainly too simple. Nevertheless, there seems to be a fairly close correspondence. A more complete study of this question might be worth while; it would show to what extent the thermodynamic functions of different electrolytes form a one-parameter family in regard to their dependence on the concentration, and give us more detailed information about the short range forces.

The assumption of short range repulsion is necessary and sufficient to explain the increase of the activity coefficients at high concentrations. The magnitude of the effect is primarily a measure for the range of the forces, as we have shown above, and the variation with the concentration is apt to be linear, no matter what the nature of the forces is. Hückel (15) suggested that the dielectric constant of electrolytes ought to decrease with increasing concentration, and he was able to show that his assumption would lead to an effect of the observed type. While this agreement is of little discriminatory value, Hückel's explanation is certainly plausible, and it seems difficult to account for the effect by any very different picture. As regards the direct evidence for the decrease of the dielectric constant, the measured variations turned out to be much larger (16) than those predicted by Hückel; but the data scatter so widely that they cannot be said to contradict a very small actual effect. A theoretical computation of the decrease in the dielectric constant to be expected from the saturation of the solvent dipoles has been made by Sack (17); again, the computed variation of the dielectric constant was much greater than what Hückel had inferred from the properties of electrolytes. My own opinion is that Hückel's relation between the dielectric constant and the thermodynamic properties of electrolytes ought to give the correct order of magnitude. If so, then it is difficult to reconcile Sack's conclusions with the observed behavior of electrolytes. Incidentally, such properties of ions as their mobilities also seem to contradict Sack's theory.

We may expect that all the various kinds of forces that are responsible for the cohesion of matter may take part in the short range interaction of ions. The forces which have been discussed here deserve special interest because they are peculiar to electrolytes, and also because they may be of somewhat greater range than ordinary molecular repulsive forces. Probably a better understanding of this phenomenon must be sought in connection with an improved theory of polar liquids. Certain properties of electrolytes seem to indicate that the electric moments of the solvent molecules are in many instances greater than is assumed by the present dipole theory.

APPENDIX

Critique of Fowler's fluctuation theory

Fowler (11) defines a function $W_{\alpha\beta}(r)$, equal to the potential of the average force acting on a pair of ions α and β at a distance r in the electrolyte. By differentiation of the Gibbs phase integral he correctly derives his equation 15, which may be written

$$\mathrm{div}_\beta\, \mathrm{grad}_\beta\, W_{\alpha\beta} - \frac{1}{kT}\, \mathrm{grad}_\beta{}^2\, W_{\alpha\beta} = \mathrm{div}_\beta\, \mathrm{grad}_\beta\, W - \frac{1}{kT}\, \mathrm{grad}_\beta{}^2\, W \qquad \text{(15F)}$$

Here, W denotes the potential energy of the entire collection of ions, that is, a function of the coördinates of all the ions in the system; the differentiations corresponding to grad_β, etc., are carried out with respect to the coördinates of the particular ion β, and the averages are taken for fixed positions of the two particular ions α and β.

Fowler now assumes that the only forces acting are Coulomb forces; this invites trouble, because then the phase integral does not converge. In order to make the phase integral convergent, one must introduce additional repulsive forces for small distances (*v. i.*).

For the moment, we grant Fowler's assumption; then the potential W of the forces obeys the relation

$$\mathrm{div}_\beta\, \mathrm{grad}_\beta\, \overline{W} = -\,(4\pi/D)\, \bar{\rho}\, e_\beta \tag{16F}$$

where $\bar{\rho}$ is an appropriate average of the charge density. Fowler obtains accordingly

$$\mathrm{div}_\beta\, \mathrm{grad}_\beta\, W_{\alpha\beta} + (4\pi/D)\, \bar{\rho}_\alpha\, e_\beta = \frac{1}{kT}\left(\mathrm{grad}_\beta{}^2\, W_{\alpha\beta} - \mathrm{grad}_\beta{}^2\, W\right) \tag{17F}$$

where $\bar{\rho}_\alpha$ denotes the mean charge density at the distance $r_{\alpha\beta}$ from the α ion.

We shall show that equation 16F cannot be correct. Consider the limiting case when the ions α and β are far apart; then

$$W_{\alpha\beta} = 0$$

together with its gradient etc., and the charge density $\bar{\rho}_\alpha$ induced by the α ion also vanishes, so that equation 16F may be written

$$0 = -\,\mathrm{grad}_\beta{}^2\, W \tag{34}$$

This equation states that there are *no forces whatever* acting on the β ion.

In order to estimate the order of magnitude of the discrepancy, we recall that, assuming electrostatic forces only,

$$-\,\mathrm{grad}_\beta\, W = E_\beta\, e_\beta$$

where E_β denotes the electric field strength (due to other ions) at the point of the ion β. The density of other ions in the neighborhood of a given ion β is certainly comparable to the mean density in the solution—probably greater—and the same holds for the mean square field. That leads us to

$$\frac{1}{kT}\,\overline{\mathrm{grad}_\beta{}^2\, W} = \frac{e_\beta{}^2}{kT}\,\overline{E_\beta{}^2} \sim \frac{e_\beta{}^2}{kT}\,\overline{E^2} = \frac{e_\beta{}^2}{kT}\,\frac{1}{V}\int E^2\, \mathrm{d}V =$$

$$= \frac{e_\beta{}^2}{DkT}\,\frac{8\pi U_{el}}{V} \sim \frac{e_\beta{}^2}{DkT}\, 4\pi \sum_\gamma \frac{e_\gamma{}^2}{D a_{\beta\gamma}}$$

The integration is performed, for a representative configuration of the other ions, over all places that are accessible to a β ion,

($r_{\beta\gamma} > a_{\beta\gamma}$), and U_{el} is the total electrostatic energy (mainly self-energy) of a system of charged spheres of radius $a_{\beta\gamma}$. Taking all $a_{\beta\gamma} = a$ we obtain, in terms of the Debye-Hückel κ,

$$\frac{1}{kT}\,\text{grad}_\beta{}^2\, W \sim \kappa^2\, e_\beta{}^2/Da \tag{35}$$

which is (according to Debye and Hückel) of the same order of magnitude as the maximum of either term in the left member of equation 17F.

If we introduce repulsive forces of short range ($= a$), so as to make the phase integral converge, we may expect reasonable results. In this case equation 16F will contain an additional term

$$\text{div}_\beta\, \text{grad}_\beta\, W_s \tag{36}$$

where W_s is the potential of the repulsive forces, and in general, W now contains W_s in addition to the electrostatic energy. It may be worth while to show more clearly the significance of the term given by formula 36; for this purpose, we chose a procedure that is very similar to Fowler's. Consider a given ion β in the field of N fixed ions, and let the energy of interaction between β and the other ions be

$$\sum^{N} \frac{e_\beta e_\nu}{r_{\beta\nu}} + u_s$$

where the function u_s is chosen in such a manner that $u = +\infty$ at all singularities and boundaries. The Coulomb energy obeys the Laplace equation; hence

$$\text{div grad}\, u = \text{div grad}\, u_s$$

We shall compute the time-average of this function on the assumption that the ion β will distribute itself among all positions according to the Maxwell-Boltzmann law. Write

$$Q = \int \exp(-u/kT)\, dV$$

then

$$Q\,\overline{\mathrm{div\ grad}\ u_s} = Q\,\overline{\mathrm{div\ grad}\ u} = \int \exp(-u/kT)\ \mathrm{div\ grad}\ u\,\mathrm{d}V =$$
$$= -\int (\mathrm{grad}\,u, \mathrm{grad}\,(\exp\,(-u/kT)))\,\mathrm{d}V = (1/kT)\int \exp(-u/kT)\ \mathrm{grad}^2\,u\,\mathrm{d}V =$$
$$= Q\,(1/kT)\,\overline{\mathrm{grad}^2\ u}$$

The difference from equation 15F is that here we have extended the averaging over the coördinates of the β ion, while in equation 15F the ions α and β are kept fixed. This difference is immaterial when α and β are far apart, because then the position of the ion β does not matter anyway; in other words, we have shown that the terms in the right member of equation 15F actually do cancel each other when $r_{\alpha\beta} = \infty$.

The above evaluation of the right-hand member of equation 15F for the trivial case $r_{\alpha\beta} = \infty$ amounts to a reversal of Fowler's derivation, and does not bring us any nearer to the real problem of computing the same quantity for finite distances $r_{\alpha\beta}$. While it is impossible to foresee what results Fowler's method might yield with the aid of new devices, its value has not been demonstrated so far.

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THE "SALTING OUT" OF NON-ELECTROLYTES FROM AQUEOUS SOLUTIONS

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The change in the solubility of a non-electrolyte in water which results from the addition of an electrolyte has been known and studied for many years. Since a decrease in the solubility of the non-electrolyte results in many instances from such salt addition the phenomenon has been called the "salting-out" effect, although there are numbers of cases in which the addition of certain salts increases the solubility of particular non-electrolytes causing them to be "salted in."

While the literature abounds with examples of data showing the effect of the addition of one or two salts on the solubility of a given non-electrolyte, comparatively few complete systematic studies of the influence of a series of salts on the solubility of a given non-electrolyte are available. Furthermore, almost no systematic studies of the effect of the molecular structure of the non-electrolyte molecule as determining the extent to which its solubility would be influenced by electrolyte additions have been made. The principal systematic investigations using a series of salts are the older work of Rothmund on phenylthiourea (1), of Hoffman and Langbeck on substituted benzoic acids (2), and of Euler on ether and ethyl acetate (3); also, the more recent investigations of Linderstrom-Lang on hydroquinone, quinone, succinic acid, and boric acid (4), of Glasstone and his coworkers on ethyl acetate and aniline (5), of Larsson on benzoic acid (6), and of Phillip Gross and his students on acetone and hydrocyanic acid (7).

Various equations have been proposed to express the relation between the change in the solubility of the non-electrolyte and the added salt concentration, but that proposed at an early date by Setschenow (8) seems to fit the data most generally and to have been most frequently employed. It is further substantiated by recent carefully determined values for the solubility of benzoic acid in aqueous potassium chloride (9). Setschenow's equation is

$$\log \frac{s_0}{s} = \log f_c = kc_s \tag{1}$$

in which s_0 and s are the solubilities of the non-electrolyte in weight units per unit volume of water and salt solution, respectively, c_s is the salt concentration in moles per liter, k is the "salting-out" constant, and f_c is the activity coefficient of the non-electrolyte expressed in concentration units. This equation is generally valid for values of c_s as high as from 2 to 3 molar, provided s_0 is small. Occasionally it is valid for salt concentrations as high as 4 molar.

The region of dilute salt solutions (below 0.5 molar) has been very little investigated, largely because of the increasing errors in the $\frac{s_0}{s}$ values. While it seems that equation 1 is the only one which will hold over an appreciable range of salt concentrations, there is some evidence that an equation of the form

$$v_a = k_1 c_s \tag{2}$$

holds for solutions of salt concentration below 0.5 molar. Here v_a is the additional volume in liters of solution which would be required to hold 1 mole of the non-electrolyte in solution, in the presence of the added salt concentration c_s, in excess of the volume of water v_0 required for its solution in the absence of the salt. Equation 2 can be shown to be an approximate limiting form of equation 1 in which $k_1 = 2.303\ v_0 k$. Data sufficiently accurate to test equation 2 in dilute solutions are not available except in a few instances. As an example there may be cited the accurate data of Chase and Kilpatrick (9) on the solubility of molecular benzoic acid in potassium chloride solutions. For potassium chloride solutions below 0.7 molar, a straight line whose equation is $v_a = 13.2\ c_s$ satisfactorily represents their data. They use equation

1 to represent the entire range of their data up to 3 molar potassium chloride solutions and calculate a value of $k = 0.138$. From this may be calculated a value for $k_1 = 12.0$ in approximate agreement with the value 13.2 found from their points in the dilute solution range. Whether equation 2 represents a simple relationship true for dilute solutions or whether it is merely an approximation form of equation 1 can only be determined by further tests with accurate data in dilute solutions. If an equation of the form of equation 2 is generally valid, it implies that one of the primary factors in "salting out" is a characteristic constancy of binding of a part of the water by at least some of the ions, the extent of which is directly proportional to the number of ions. The water so bound is probably removed as a shell of oriented water dipoles around the ion. These become unavailable as solvent molecules in which the non-electrolyte could be dispersed, and so it is necessary to add more solution in order to retain a mole of non-electrolyte in molecular dispersion in the salt solution at the temperature concerned.

Probably because of the limited range of solutes investigated, the opinion has at times been held that the "salting-out" effect is not influenced greatly by the character of the non-electrolyte. That this is quite erroneous may be seen when we consider the solubility of a diverse series of non-electrolytes in a given salt solution as in table 1 (10). In this table the weight per cent of non-electrolyte "salted out" (referred to 1000 g. of water in each case) is compared with such measures of its polar character as its dielectric constant D as a liquid, its dipole moment μ, and total polarization P as determined in dilute solution in non-polar solvents.

While there is no consistent correlation shown, there is a well-defined trend in the extent of salting out with polar properties in such direction that those substances which are more polar are least salted out from this electrolyte solution of fixed ion population and kind. This correlation finds recognition in the theory of the "salting-out" phenomena proposed by Debye and McAulay (11) and Debye (12). This theory pictures the "salting-out" effect as a consequence of the aggregation of the water molecules of greater polarity around the ions owing to the field of the latter. The less polar non-electrolyte molecules tend to congregate in the portions of the solution most remote from the field of the ions, with the net result that an enhancement of the water molecules around the ions and of the non-electrolyte in the solution regions away from the ions occurs. A reduction of the solubility of the non-electrolyte, referred to the total water present, thus results, due to the increase of non-electrolyte–water ratio in those regions of the solution containing the non-electrolyte. The criterion of polarity which Debye employs is the dielectric constant of the saturated aqueous solution of the non-electrolyte relative to water at the same temperature. On this basis if the saturated solution has a dielectric constant less than water, "salting out" occurs in the presence of the added salt. If the dielectric constant of the saturated non-electrolyte solution is above that of water, the non-electrolyte becomes more soluble in the salt solution or is

TABLE 1

Salting out by 0.5 molal potassium chloride at 30°C.

	PER CENT SALTED OUT	D	P (Total polarization)	$\mu \times 10^{18}$
p-Nitroaniline	3.0		1080	7.1
m-Dinitrobenzene	3.0		338	3.8
Nitrobenzene	3.1	36.4	346	4.0
Monobromobenzene	4.1	5.3	82	1.50
Monochlorobenzene	5.6	10.9	82	1.56
Bromoform	8.2	4.4	51	1.0
Methylene bromide	9.1	7.0	61	1 4
Chloroform	9.7	5.1	51	1.2
Ethylene chloride	11.3	10.4	93	1.8
Methylene iodide	11.6	5 5	58	1.1
n-Propyl bromide	11.9	7.2	103	1.9
n-Butyl bromide	12.3	6.6	114	1.9
n-Propyl iodide	13.2		102	1.7
Ethyl iodide	13.5	7.4	86	1.7
Ethylene bromide	13.7	4.8	68	1.0
Carbon tetrachloride	16.7	2.23	28	0
Benzene	19.1	2.26	26	0
Toluene	24.3	2.39	36	0

"salted in." This means that the non-electrolyte tends to aggregate around the ions at the expense of the water, and so the non-electrolyte–water ratio in regions removed from the ions is lowered and the total water present can hold more non-electrolyte in solution. A test of this theory involves a knowledge of the dielectric constant of the saturated aqueous non-electrolyte solution,—information which to date is available in but a few instances.

The best test of the theory is provided by the data of Phillip Gross and his coworkers (7) on the solubility of acetone and hydrogen cyanide in aqueous salt solutions. The former lowers while the latter raises the dielectric constant of water. In agreement with the predictions of the theory, acetone is "salted out" whereas hydrogen cyanide is "salted in." The "salting-out" effects calculated from the theory agree in order of magnitude (13) with those found experimentally, although actual values only roughly approximate the observed percentages "salted out" for the different salts. It is clear, however, that such agreement as to order of magnitude would not result unless the Debye picture for the mechanism was essentially correct and represented at least a significant part of the "salting-out" effect. The possibility of other factors also entering into the effect is of course not precluded, as Debye himself clearly points out (14). A study of the recent data on "salting out," particularly in relation to the additive effects of ions, indicates the possible nature of such factors.

It has been generally recognized wherever data on a sufficient number of salts were available for a test that the effects of the positive and negative ions of an electrolyte were at least approximately additive. This is clearly brought out by the data of Larsson for benzoic acid which include a large number of salts (6). Assuming the validity of this additivity principle Larsson writes for equation 1

$$\log f_c = kc_s = (k_c + k_a)c_s \tag{3}$$

in which k_c is the salting-out constant for the cation, and k_a that for the anion. Comparison of his values for a series of chlorides and nitrates of the same metals showed a constant difference due to the difference in the value of k for the chloride and nitrate ion.

In order to evaluate the separate values of k_c and k_a he makes the arbitrary assumption that $k_{K^+} = k_{Cl^-}$ and from the value $k = 0.14$ for potassium chloride thus finds $k_{K^+} = 0.07$. From these values and those for the respective salts he calculates the values for the other ions. These are reproduced in table 2 taken from his paper (6), as they illustrate the range of such values as well as do any other data and they cover a wide variety of salts.

This table further illustrates a general regularity in all "salting-out" data, that of the effect of ionic size. With but rare exceptions the extent of "salting out" by a series of salts of the same valence type containing a common ion is in inverse order to the size of the cation, thus, for example, Li > Na > K > Rb > Cs. The same regularity holds for the simple anions, i.e., Cl > Br > I. This effect of ionic size has been recognized as a necessary and integral part of any theory of "salting out." Thus for the "salting out" of acetone by uni-univalent electrolytes the Debye equation (12) reduces to (13)

TABLE 2

Salting-out constants of individual ions for benzoic acid

ION	k	ION	k	ION	k	ION	k
H^+	0.02	Cs^+	−0.08	Cl^-	0.07	$-OCOCHCl_2$	−0.14
Li^+	0.12	Mg^{++}	0.10	Br^-	0.00	$-OCOCCl_3$	−0.12
Na^+	0.11	Ca^{++}	0.10	I^-	−0.02	$-OCOC_6H_5$	−0.32
K^+	0.07	Sr^{++}	0.09	NO_3^-	0.03	$-OSO_2C_6H_5$	−0.23
Rb^+	0.02	Ba^{++}	0.08	ClO_4^-	0.06	$-OSO_2C_{10}H_7$ (β)	−0.86

$$\frac{1}{fc} = 1 - \frac{0.27}{a} c_s \tag{4}$$

where a is the average ionic radius in Ångström units. In this as in other cases there is the difficulty of properly evaluating the radius "a", and as this has to be done from other solution data only an average value is obtained and not the independent contribution of the size of each ion to the total "salting out."

While it is true that there are but few exceptions to the regularities just noted there are a number of cases which involve an anomalous effect of a different kind. These are those instances in which the addition of certain salts to water increases the solubility of the non-electrolyte, whereas others decrease it. Thus Linderstrom-Lang found that whereas sodium and lithium chlorides "salted out" boric acid, potassium, rubidium, and cesium chlorides salted it in. These are not explicable on the basis of the raising of the dielectric constant of water as in the case of the "salting in" of hydrogen cyanide, which is a true inversion of the "salting-out" effect in the sense of the Debye theory previously outlined. The same non-electrolyte cannot both raise and lower the dielectric constant of water at a given concentration. It is therefore clear that these anomalies must originate at least in part from the electrolyte. In general they have been noted and then classified as abnormal and attributable to specific interaction effects, with the non-electrolyte concerned, of the iodides, chlorates, nitrates, and similar ions for which they occur. They show in spite of this anomalous effect the same regularities of the order in which they affect solubility as previously noted. Thus the "salting-in" effect, for instance, in the case of succinic acid decreases in the order $CsCl > RbCl > KCl$. Furthermore it is difficult to conceive of the otherwise normal salts—potassium, rubidium and cesium chlorides—as behaving in some abnormal manner in this particular case. Likewise from Larsson's results we note that cesium chloride shows a slight "salting-in" effect. To indicate that this effect is fairly general and not confined to substances of the type of weak acids whose ionization equilibria might play some part in it, some data for benzene and nitrobenzene are cited here (15). If the values of f_m, the activity coefficient for molalities, are considered for $c_s = 1\ M$, it is found that benzene is "salted out" largely by potassium chloride and very little by cesium chloride, and is "salted in" moderately by potassium benzoate. Nitrobenzene is "salted out" less than half as much as benzene by potassium chloride, slightly "salted in" by cesium chloride, and largely "salted in" by potassium benzoate. By comparison with Larsson's table it will be seen that this is in approximate accord with his results for benzoic acid. This anomalous "salting-in" effect is most evident for salts with large negative ions but is not confined to them alone, as shown by the instances of the three alkali chlorides and succinic acid.

Since this effect occurs in some cases even with such relatively small negative ions as chlorides, its explanation must be more fundamental than that of an abnormal specific interaction. If Larsson's table is used as an illustration and the principle of additivity is assumed, a basis for correlating all the effects is possible. Larsson assumed arbitrarily that $k_{K^+} = k_{Cl^-} = 0.07$ and then calculated that $k_{Cs^+} = -0.08$, because k for cesium chloride was found to be -0.01. If the arbitrary assumption that $k_{K^+} = k_{Cl^-}$ had any significance it would imply that cesium ion was "salting in" the benzoic acid. However, if it is assumed that the slightly increased solubility in cesium chloride is the result of the near balance of two opposite effects, either of the ions could be thought of as responsible for the "salting in." Since the "salting-in" anomaly is more common for salts with large negative ions, it seems reasonable to attribute the "salting-in" effect to the chloride and not to the cesium ion. On this basis the result for cesium chloride is the consequence of the slight inequality in the operation of two practically equal and opposite effects, "salting out" by the cation and "salting in" by the anion.

In the general case these opposite effects will not counterbalance each other, either the "salting out" due to the cation or the "salting in" due to the anion predominating and so determining the direction of the net effect observed for the salt in question. Such an assumption accounts for the anomalies noted above, meets the requirements of the additivity principle, and agrees also with the observed order of increasing "salting out" in a series of salts with a common anion from cesium to lithium. The decreasing "salting out" for a similar series with the anions Cl^-, Br^-, I^- under this assumption is interpreted to mean that the "salting in" by these ions increases with their size. This is in general agreement with the results of Larsson for the large negative organic ions though an additional factor, that of the lack of spherical symmetry, probably also enters in these cases.

An attempt to picture the mechanism underlying such an antagonistic action of cation and anion in their effects on the solubility of non-electrolytes is worth while, though it must be in large degree speculative. The action of the cation is regarded as essentially unaltered from that given by the Debye theory, namely, one of aggregation of water dipoles immediately around the cation and of enhancement of non-electrolyte molecules in regions removed from the cation with the consequent "salting out." In the region around the anion, non-electrolyte molecules must aggregate and water molecules decrease. This does not necessarily imply an absence of binding of water molecules, but does imply a binding of a different order of magnitude than in the case of the cation and one more easily displaced by, or at least shared with, the non-electrolyte. There is an accumulation of related evidence for the existence of such a difference in what is usually termed the "degree of hydration" of cations and anions, the amount of water bound to the former exceeding that bound to the latter. Perhaps the strongest evidence for this is from transference experiments such as those of Washburn (16). These showed that the least hydrated cesium ion carries more water than does the chloride ion. Sugden (17) arrives at the same general conclusion as to the existence of this difference, but goes so far as to say that the anions are unhydrated. This seems doubtful, however, at least in the case of such a small ion as the fluoride ion, for instance.

The reason for aggregation of the non-electrolyte molecules about the anion is more difficult to see, at least for the simple spherical ions such as the halogens. For the complex ions this is not so difficult. An ion like the benzoate ion consists of a large non-polar phenyl group with a small complex carboxyl group of high dipole moment concentrated at one end where the ionic charge resides. The field around such an ion will be highly unsymmetrical, being localized and intense for a small region at one end and low or practically absent at the other. In the space around such ions there would be a small region adjacent to the carboxyl group in which water molecules tended to congregate to some extent. In the proximity of the phenyl group the less polar molecules of the non-electrolyte would tend to accumulate, leaving regions remote from the ion poorer in these and richer in water. The size of the ion and relative distribution of the more and less polar portions of the field about it, together with possibilities for orientation inherent in the non-electrolyte molecule, will result in the highly specific character of the solubility effects which are observed.

Finally it must be emphasized that this assumption of the antagonistic action of the two ions, the cation "salting out" and the anion "salting in," while it seems to fit the observations now extant, may have to be modified in particular cases as the range of ions and non-electrolytes studied is increased. Concerning the behavior in "salting-out" phenomena of complex positive ions of large size but little is known. It seems possible that cases will be found where these, because of their dissymmetry, might tend to orient particular non-electrolytes around them at the expense of water and so "salt in" the non-electrolytes. Furthermore no mention in the foregoing has been made of cases of polyvalent ions as these involve the added problem, in all but the most dilute solutions, of the effect of ionic interaction. The need for data in the dilute solution range is seen to be necessary before much further progress in this direction can be made.

SUMMARY

A survey of the data of the "salting-out" phenomenon has been made and the presence of regularities such as the principle of additivity of individual ionic effects noted. The existence of certain anomalies of general occurrence has also been pointed out.

To explain these a theory of the antagonistic action of cation and anion is proposed and reasons advanced which make it seem probable that the cation is responsible for the "salting-out" portion and the anion for the "salting-in" portion of the effect. According as one or the other predominates, in the case of a given electrolyte, a net observed "salting out" or "salting in" of a given non-electrolyte will result.

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THE COMPLETE CALCULATION OF ACTIVITY COEFFICIENTS FROM FREEZING POINT DATA

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Despite the importance of the freezing point method for the calculation of activity coefficients, it has not yet been made to yield results of high precision. For their well-known application of the method to sodium chloride solutions, Lewis and Randall (1) were forced to use data very limited in range and accuracy. In addition to experimental uncertainties, they permitted several simplifying approximations to enter their calculations.

It is the purpose of this investigation to examine the various approximations; to remove those not permissible in a precise calculation; to introduce into the calculation heat of dilution data recently made available; to discuss the precision of the calculation as a whole; and finally, to point out possible sources of remaining errors. The difficulty of the extrapolation of Lewis and Randall's j function to infinite dilution is not discussed in this paper. The problem of extrapolation has been treated for potassium chloride solutions by Spencer (2) with a method which Scatchard (3) has found to agree well with his recent measurements.

Our needs will be adequately met by a calculation of the ratio of the activity coefficient, γ, to the value of γ at 0.1 molal. Harned and Nims (4) have determined this ratio, $\gamma/\gamma_{0.1}$, by means of electromotive force measurements. In table 1, column 4, their data at 25°C. are presented for comparison with the activity coefficients calculated from freezing points. In the second column are tabulated values of $\gamma'/\gamma'_{0.1}$ calculated from γ', the "provisional values" obtained by Lewis and Randall when they neglected heats of dilution. In the third column are values of

$\gamma/\gamma_{0.1}$ derived from their "final values" of the activity coefficient, γ. If the electromotive force results are not greatly affected by dissolved electrode materials or side reactions, Lewis and Randall's $\gamma/\gamma_{0.1}$ for a 4 molal solution is about 6 per cent in error.

Since the freezing point method does not involve such uncertainties as side reactions, dissolved electrode materials, etc., it is very important that its precision be improved as much as possible. The development of the following equations is necessary.

TABLE 1

Activity coefficients from various sources

The first line of initials indicates sources of activity coefficients; the second, sources of freezing point data; the third, sources of relative heat contents. The last line in the table shows the per cent deviation at 4 molal from the results of Harned and Nims, adopted as a tentative standard.

	$\gamma'/\gamma'_{0.1}$	$\gamma/\gamma_{0.1}$	$\gamma/\gamma_{0.1}$	$\gamma/\gamma_{0.1}$	$\gamma/\gamma_{0.1}$
γ ϑ x	L + R L + R . .	L + R L + R L + R	H + N	Y L + R Y + M	Y I. C. T. Y + M
M					
0.2	0.940	0.942	0.940	0.944	0.942
0.5	0.855	0.863	0.873	0.871	0.871
1.0	0.789	0.815	0.843	0.827	0.839
2.0	0.768	0.828	0.860	0.845	0.851
3.0	0.786	0.882	0.924	0.901	0.908
4.0	0.823	0.959	1.017	0.978	0.988
Per cent..	19	5.7	(0.0)	3.8	2.9

Let the molal heat capacity of ice minus that of water be represented as a function of *Centigrade* temperature, thus:—

$$\Delta C_p = \Delta\Gamma_0 + \Delta\Gamma_1 t + \Delta\Gamma_2 t^2 + \Delta\Gamma_3 t^3 \tag{1}$$

Then the molal heat of solidification, ΔH_s, is given by the following expression, in which ΔH_Θ represents its value at the freezing point, Θ, of the solvent.

$$\Delta H_s = \Delta H\Theta + \Delta\Gamma_0 t + \frac{\Delta\Gamma_1 t^2}{2} + \frac{\Delta\Gamma_2 t^3}{3} + \frac{\Delta\Gamma_3 t^4}{4} \tag{2}$$

Adopting the procedure and symbols of Lewis and Randall (p. 282 et seq.), but retaining more terms in our series, we obtain the following two equations for the temperature variation of the activity of the solid solvent, a_s. The symbols and those of subsequent equations are explained in table 2.

TABLE 2

Explanation of symbols

$$A_1 = \frac{\Delta H_\Theta}{R\Theta^2} = -\frac{1}{55.508\ \lambda}$$

$$B_1 = 2\frac{\Delta H_\Theta}{R\Theta^3} - \frac{\Delta\Gamma_0}{R\Theta^2}$$

$$C_1 = 3\frac{\Delta H_\Theta}{R\Theta^4} - 2\frac{\Delta\Gamma_0}{R\Theta^3} + \frac{\Delta\Gamma_1}{2R\Theta^2}$$

$$D_1 = 4\frac{\Delta H_\Theta}{R\Theta^5} - 3\frac{\Delta\Gamma_0}{R\Theta^4} + \frac{2}{2}\frac{\Delta\Gamma_1}{R\Theta^3} - \frac{\Delta\Gamma_2}{3R\Theta^2}$$

$$E_1 = 5\frac{\Delta H_\Theta}{R\Theta^6} - 4\frac{\Delta\Gamma_0}{R\Theta^5} + \frac{3}{2}\frac{\Delta\Gamma_1}{R\Theta^4} - \frac{2}{3}\frac{\Delta\Gamma_2}{R\Theta^3} + \frac{\Delta\Gamma_3}{4R\Theta^2}$$

$$B_2 = -\frac{55.508}{2.3026}B_1 \qquad D_2 = -\frac{55.508}{2.3026}D_1$$

$$C_2 = -\frac{55.508}{2.3026}C_1 \qquad E_2 = -\frac{55.508}{2.3026}E_1$$

$$\mathrm{d}\ln a_s = (A_1 + B_1\vartheta + C_1\vartheta^2 + D_1\vartheta^3 + E_1\vartheta^4 + \dots)\,\mathrm{d}\vartheta \tag{3}$$

$$\mathrm{d}\ln a_s = A_1\mathrm{d}\vartheta + B_1\vartheta\mathrm{d}\vartheta + \frac{C_1\vartheta\mathrm{d}(\vartheta^2)}{2} + \frac{D_1\vartheta\mathrm{d}(\vartheta^3)}{3} + \frac{E_1\vartheta\mathrm{d}(\vartheta^4)}{4} + \dots \tag{4}$$

From these we derive equation 5 for the calculation of the activity of the solvent, a_1'', at any specified temperature, and equations 6 and 7 for the evaluation of γ, the activity coefficient of the solute at the same temperature.

$$2.3026\log a_1'' = \left(A_1\vartheta + \frac{B_1\vartheta^2}{2} + \frac{C_1\vartheta^3}{3} + \frac{D_1\vartheta^4}{4} + \frac{E_1\vartheta^5}{5} + \dots\right) + 2.3026x \tag{5}$$

$$\log \gamma = -\int_0^m j \,\mathrm{d} \log m - \frac{j}{2.3026} + \frac{1}{\nu} \int_0^m \frac{(B_2\vartheta + C_2\vartheta^2 + D_2\vartheta^3 + E_2\vartheta^4 + \ldots)}{m} \,\mathrm{d}\vartheta - \frac{55.508}{\nu} \int_0^m \frac{\mathrm{d}x}{m} \tag{6}$$

$$\log \gamma = -\int_0^m j \,\mathrm{d} \log m - \frac{j}{2.3026} + \frac{B_2}{\nu} \int_0^m \frac{\vartheta}{m} \,\mathrm{d}\vartheta + \frac{C_2}{2\nu} \int_0^m \frac{\vartheta}{m} \,\mathrm{d}(\vartheta^2) + \frac{D_2}{3\nu} \int_0^m \frac{\vartheta}{m} \,\mathrm{d}(\vartheta^3) + \frac{E_2}{4\nu} \int_0^m \frac{\vartheta}{m} \,\mathrm{d}(\vartheta^4) + \ldots - \frac{55.508}{\nu} \int_0^m \frac{\mathrm{d}x}{m} \tag{7}$$

Values adopted for the various physical constants used in this investigation are given below. The substitution of these data for those used by Lewis and Randall results in a slightly increased discrepancy at 4 molal. The author is indebted for these estimates to a recent study made by Spencer (5).

$\Theta = 273.18$ degrees,

$R = 1.9864$ cal. mole^{-1} deg.$^{-1}$,

$\lambda = 1.858_8$ kilogram deg. mole^{-1},

$\Delta H_\Theta = -\ 1436._7$ cal. mole^{-1},

$\Delta\Gamma_0 = -\,9.04_9$ cal. mole^{-1} deg.$^{-1}$,

$\Delta\Gamma_1 = 0.05_{66}$ cal. mole^{-1} deg.$^{-2}$, … $\Delta\Gamma_2 = \Delta\Gamma_3 = 0$.

The approximations which Lewis and Randall allowed to enter their calculations may be summarized as follows;—

1. Treatment of ΔC_p as a constant, which implies the omission of all terms after the second in equation 2;
2. Omission of all terms between the third and last of equation 7;
3. Treatment of $\bar{L}_1$ as a linear function of temperature.

The first two of these may be discussed together, since the terms omitted from equation 2 affect only the C, D, E, (and higher) terms of the series in equation 7. The importance of the C, D, and E terms may be illustrated with a few examples. Table 3 shows the per cent by which the calculated value of γ is reduced by each of the terms. The discrepancy between the freezing point and electromotive force methods is not reduced by the use of the temperature variation of ΔC_p and the introduction of the extra series terms, but is increased slightly. However, at least the C_2 term must be used for the calculation of γ when a precision of a few tenths of one per cent is required.

In an investigation of the temperature variation of $\bar{L}_1$ recently conducted in this laboratory (6, 7), measurements were made at 25°, 12.5°, and 0°C. Values read from three plots of $\bar{L}_1$ versus molality are shown in figure 1. They are connected by solid lines corresponding to quadratic equations derived to represent the data. Dotted lines represent extrapolations of these equations to the freezing points of the respective solutions.

TABLE 3

Effect of terms on calculated values of γ

TERM CONTAINING	4.0 MOLAL NaCl	5.2 MOLAL NaCl
C_2	0.28 per cent	0.58 per cent
D_2	0.02 per cent	0.06 per cent
E_2	0.001 per cent	0.006 per cent

The determination of x from these data is illustrated by the following example for a 4.45_8 molal solution.

$$\bar{L}_1 = 21.1_6 - 1.02_9\,(t - 25) + 0.008_{93}\,(t - 25)^2 \tag{8}$$

$$\log \frac{a_1''}{a_1'} \equiv x = -21.1_6 y - 1.02_9 z - .017_9 \Omega \tag{9}$$

The terms y and z are defined by Lewis and Randall (p. 349) and

$$\Omega = 298.18\left(z + \frac{t' - 25}{2}\,y\right) \tag{10}$$

According to equation 9, $x = -.00603$. If the last term is neglected, $-.00534$ is obtained for x.

In the fifth column of table 1 is $\gamma/\gamma_{0.1}$ derived from these x values and the j values of Lewis and Randall. In the sixth column are activity coefficient data determined from these same x values, and from the freezing point data listed in International Critical Tables (8). Spencer's constants and the C_2 term of equation 7 were employed in this calculation, though the discrepancy was thus increased. For the 4 molal solution the difference between the electromotive force data and the freezing point method has been reduced from nearly 6 per cent to about 3 per cent.

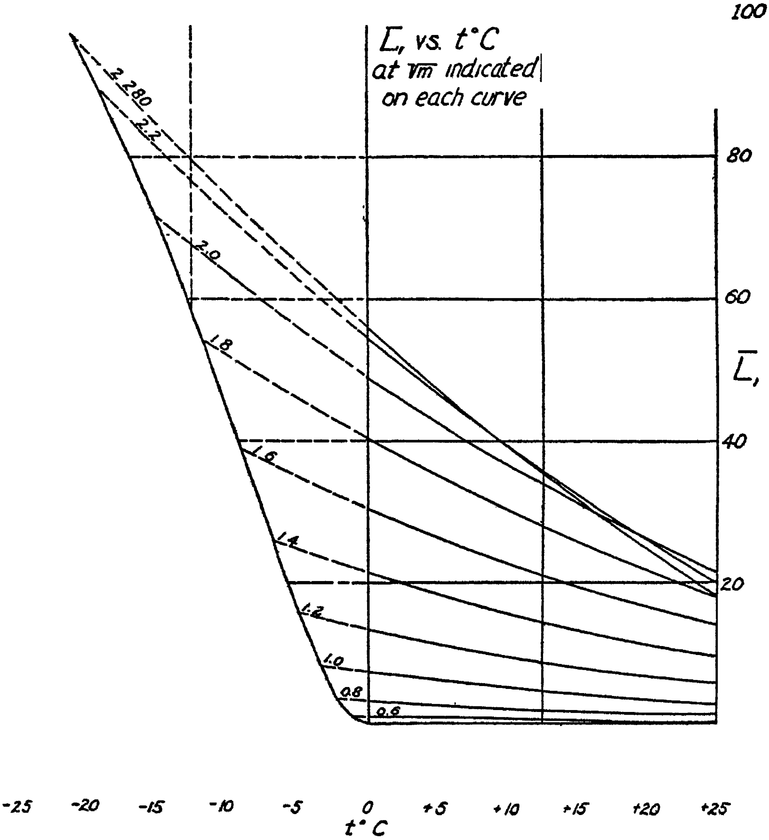

FIG. 1. RELATIVE PARTIAL MOLAL HEAT CONTENTS

The discrepancy is still larger than it should be, and the data must be examined to reveal the cause. For this purpose, the following equation is useful.

$$\log\left[\left(\frac{\gamma'}{\gamma'_{0.1}}\right)\left(\frac{m}{0.1}\right)\right] = -\frac{55.508}{2.3026\,\nu R}\int_{0.1}^{m}\frac{\Delta H}{mT^2}\,d\vartheta \qquad (11)$$

According to table 1, column 2, the logarithm in the left side of this equation is about 1.5 for a 4 molal solution. An error of 0.1 per cent in R, or an average 0.1 per cent error in ΔH or T^2 would produce the same per cent error in this logarithm, i.e., an error of 0.0015. Log $(\gamma/\gamma_{0.1})$ would be affected by the same amount and an error of 0.3_5 per cent would therefore be introduced into $\gamma/\gamma_{0.1}$.

The probable error in ΔH_Θ according to the estimate in International Critical Tables (9) is 0.10 per cent. An error of this magnitude would introduce into ΔH an error varying from 0.10 per cent to 0.12 per cent and, therefore, one of about 0.4 per cent into $\gamma/\gamma_{0.1}$ at 4 molal. The error in ΔC_p is not likely to be important in comparison with this hypothetical error in ΔH_Θ; a change in $\Delta\Gamma_0$ greater than 1 per cent would be required to affect the B_2 term and higher terms sufficiently to produce a variation of 0.1 per cent in γ at 4 molal.

The probable error in R, according to Birge (10), is too small to affect materially the precision of the activity coefficient calculation. The probable error in Θ^2, Birge estimates, is about 0.022 per cent, which produces a probable error in T^2 of 0.022 per cent to 0.024 per cent. This also would add very little to the uncertainty in $\gamma/\gamma_{0.1}$. Further errors in T^2 are caused by errors in ϑ, which are discussed below.

A thoroughly satisfactory calculation requires measurements of $\bar{L}_1$ below 0°C. Such data might be introduced into the calculation by the incorporation of a fourth term in equations of the type of 8 and 9. The third term introduced a correction into γ at 4 molal of only 2.1 per cent. Probably the three terms represent the $\bar{L}_1$ curve so well that a fourth term would have little further effect.

The greatest uncertainty in the calculation seems to lie in the freezing point data. A systematic error of 1 per cent in ϑ would imply a constant error of 1 per cent in $d\vartheta$ of equation 11 together with a small additional error (always less than 0.2 per cent) in

T^2. The remaining discrepancy of about 3 per cent could be caused therefore by an average error of about 0.8 per cent in ϑ.

An example of existing discrepancies in freezing point data is shown in the following values of ϑ for a 1 molal solution.

ϑ used by Lewis and Randall = 3.33
ϑ of International Critical Tables = 3.37
ϑ Scatchard (3) = 3.39

In International Critical Tables (8) only one investigation of freezing points of sodium chloride solutions more concentrated than 1.2 molal is listed. The data of this series were adopted for concentrated solutions, although the value of ϑ given for a 1 molal solution is 1.2 per cent smaller than that selected for the Tables to represent all of the significant data in this region. New measurements of freezing points of concentrated solutions will probably reduce much further the discrepancy between the freezing point calculations and the electromotive force data of Harned and Nims (4). These measurements with further investigations of $\bar{L}_1$ at low temperatures may soon reduce the uncertainty in $\gamma/\gamma_{0.1}$ close to the 0.4 per cent due to the probable error in ΔH_{Θ}.

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THE APPARENT MOLAL HEAT CAPACITY, VOLUME, AND COMPRESSIBILITY OF ELECTROLYTES

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INTRODUCTION

For the last fifty years, a great number of investigators have studied the activity of electrolytes in solution. Arrhenius' theory and the more recent interionic attraction theory were designed primarily to explain this property, yet any completely satisfactory solution theory must explain *all* properties of solutions. The Debye-Hückel theory has now been extended to explain the change of viscosity, conductivity, heats of dilution, and other properties of solutions of electrolytes. The validity of its basic postulates is strengthened by each such successful extension. All of these properties approach the simple laws demanded by theory only at *extremely low* concentration. In contrast to this, the three apparent molal properties which we will discuss exhibit simple relationships over the *whole range* of concentration. We will first present the experimental facts which show the similarity of the behavior of these properties and will then see how far our theories can explain this relationship. The correct interpretation of these facts must eventually lead to a more complete and satisfactory theory of solutions.

An *apparent molal property* of the solute may be defined by the equation:

$$\Phi(G) = \frac{G - n_1\overline{G}_1^0}{n_2} \tag{1}$$

where G is any extensive property of a solution, $\overline{G}_1^0$ the corresponding molal property of the solvent, and n_1 and n_2 the number of moles of solvent and solute. Thus if we take a volume, V, of solution which contains *one mole* of solute, the apparent molal volume of the solute is equal to V minus the volume, V_1, of the water which is used in making up the solution:

$$\Phi(V_2) = V - V_1 \tag{2}$$

Equation 2 shows us that the error in $\Phi(V_2)$ becomes larger as V increases, being nearly inversely proportional to the concentration c. This is true of any apparent molal property. The particular extensive property of the solution must be studied with great precision in order to determine with any certainty the value of Φ in dilute solutions.

APPARENT MOLAL HEAT CAPACITIES

Within the last four years several workers have studied the heat capacities of aqueous solutions of many typical electrolytes at 25°C. over a wide concentration range. These data are sufficiently accurate to furnish, even in fairly dilute solutions, satisfactory values of the apparent molal heat capacity defined by the equation

$$\Phi(C_{p_2}) = s\left[\frac{1000}{m} + M_2\right] - \frac{1000}{m} \tag{3}$$

where s is the specific heat of the solution, m is the molality (moles of solute per 1000 g. of water), and M_2 is the molecular weight of the solute.

Randall and Rossini (1), from a careful study of the heat capacities of a number of solutions, confirmed the earlier statement of Randall and Ramage (2) that the apparent molal heat capacity is a linear function of $m^{\frac{1}{2}}$ from the lowest concentration studied up to about 2 molal. Work in this laboratory (3) has shown that this linear relationship undoubtedly holds in the case of five other uni-univalent electrolytes from 2 molal to about 0.2 molal. There is some uncertainty about the more dilute range. A marked departure from linearity was observed by Gucker and Schminke (3a) in the case of two solutes (potassium hydroxide and hydrochloric acid) below 0.2 molal. Similar irregularities in the very dilute range have been noted by La Mer and Cowperthwaite (4) and by Young (5). La Mer and Cowperthwaite studied the E.M.F. of suitable cells over a wide range of temperature and calculated $\overline{C}_{p_2}$[1] for zinc sulfate below 0.01 molal. They conclude that even as low as 0.0005 molal it is not a linear function of $m^{\frac{1}{2}}$. Young calculated the apparent molal heat capacity of sodium chloride in very dilute solutions from a determination of the heat of dilution at two different temperatures and concluded that for this salt also Φ is not a linear function of $m^{\frac{1}{2}}$ in very dilute solutions. An exact determination of the limiting law for apparent molal heat capacity must await precise data for a large number of electrolytes in the very dilute range. The necessary accuracy cannot be realized by direct determination of the specific heat, but undoubtedly can be obtained by a study of the temperature coefficient of the heat of dilution. Such a study is being continued by Professor Young at the University of Chicago and is also being carried out in this laboratory by a slightly different procedure.

Despite the uncertainty in the very dilute range, linear extrapolation of the apparent molal heat capacity curves gives values at infinite dilution which are additive for the ions. This does not, of course, prove that the extrapolation is correct, since all of the lines might show similar curvature in the very dilute range. It is interesting to note that the additivity of apparent ionic heat capacities at infinite dilution was shown thirty years ago by Lamb (6) from a study of the rather meager data in the literature at that time.

Some other interesting generalizations now emerge. While the apparent molal heat capacity of non-electrolytes or weak electrolytes is *positive*, that of all strong electrolytes in dilute solutions is *negative*. A comparison of different salts shows that those of higher valence type have progressively more negative values of Φ^0 and progressively steeper slopes against $m^{\frac{1}{2}}$. We have plotted in figure 1 a number of typical apparent molal heat capacity curves which illustrate the general principles discussed above. We have

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[1] $\overline{C}_{p_2} = \left(\frac{\partial \overline{C}_p}{\partial n_2}\right)_{n_1}$, the *partial* molal heat capacity of the solute. Partial and apparent molal quantities are equal at zero concentration and proportional in the dilute range (cf. equation 17). Their conclusions regarding $\overline{C}_{p_2}$ therefore apply also to $\Phi(C_{p_2})$.

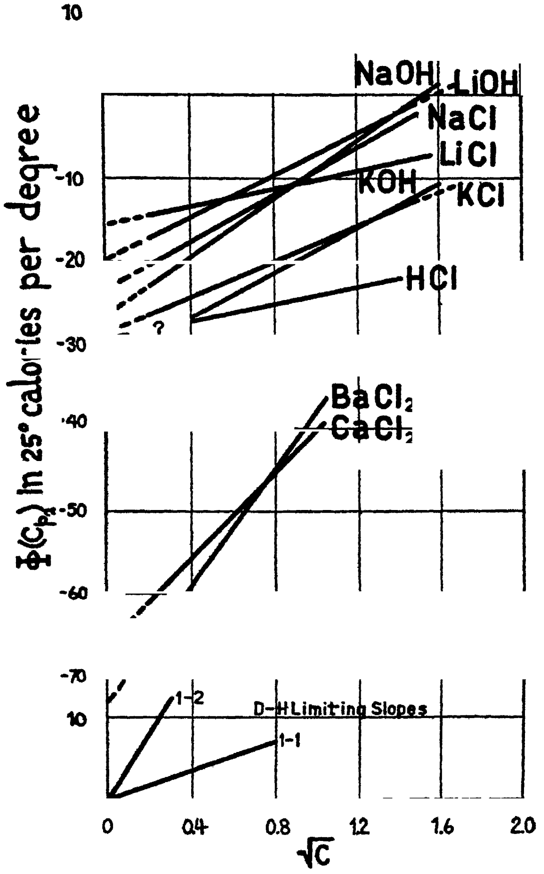

FIG. 1. APPARENT MOLAL HEAT CAPACITIES AT 25°C.

used as abscissa $c^{\frac{1}{2}}$ (which is nearly proportional to $m^{\frac{1}{2}}$ at low concentration), in order to make these lines strictly comparable with those in other figures.

Rossini (7) has made a careful survey of the literature and has calculated the apparent molal heat capacity of nearly all the salts for which sufficiently accurate heat capacity data were available. As he has shown, these values are a most concise and accurate way of representing heat capacity data and the linear relationship is very convenient for interpolating and extrapolating such data.

APPARENT MOLAL VOLUMES

The apparent molal volume of a solute is most conveniently calculated from the density of the solution, using the equation

$$\Phi(V_2) = \frac{1000}{c}\left(\frac{d_1 - d}{d_1}\right) + \frac{M_2}{d_1} \tag{4}$$

where c is the concentration in moles per liter, and d and d_1 are the density of the solution and of pure water. This function has been studied for a long time and values of Φ are tabulated in Landolt-Börnstein, but it was only in 1929 that Masson (8) discovered that for most electrolytes Φ is a linear function of $c^{\frac{1}{2}}$. The experimental evidence has been studied very carefully by Scott (9) and also by Geffcken (10), who made additional density measurements in very dilute solutions. Both authors conclude that the linear relationship is valid for most of the univalent electrolytes studied, though a number of the lines, particularly those for lithium salts, show an appreciable deviation from the linear relationship in fairly concentrated solutions. Linear extrapolation of Φ for the alkali halides at many different temperatures was shown by Geffcken and Scott to indicate additive apparent ionic volumes at infinite dilution. Linear extrapolation of Φ from moderate concentrations (0.2 c) also gave results which were in good agreement with the values obtained by Lamb and Lee (11), who studied the density of sodium, lithium, and potassium chloride solutions down to 0.0001 c by means of an ingenious sinker method.

Masson, Geffcken, and Scott all concluded that the linear relationship held for any given electrolyte up to a high concentration, but that the slopes were appreciably different for individual electrolytes of the same valence type. On the other hand, Redlich and Rosenfeld (12) concluded from an examination of the best experimental data that the lines were all curved at high concentration and approached the *same slope* at great dilution. Which of these two views is correct can only be decided by further extremely precise density measurements, particularly in the dilute range.

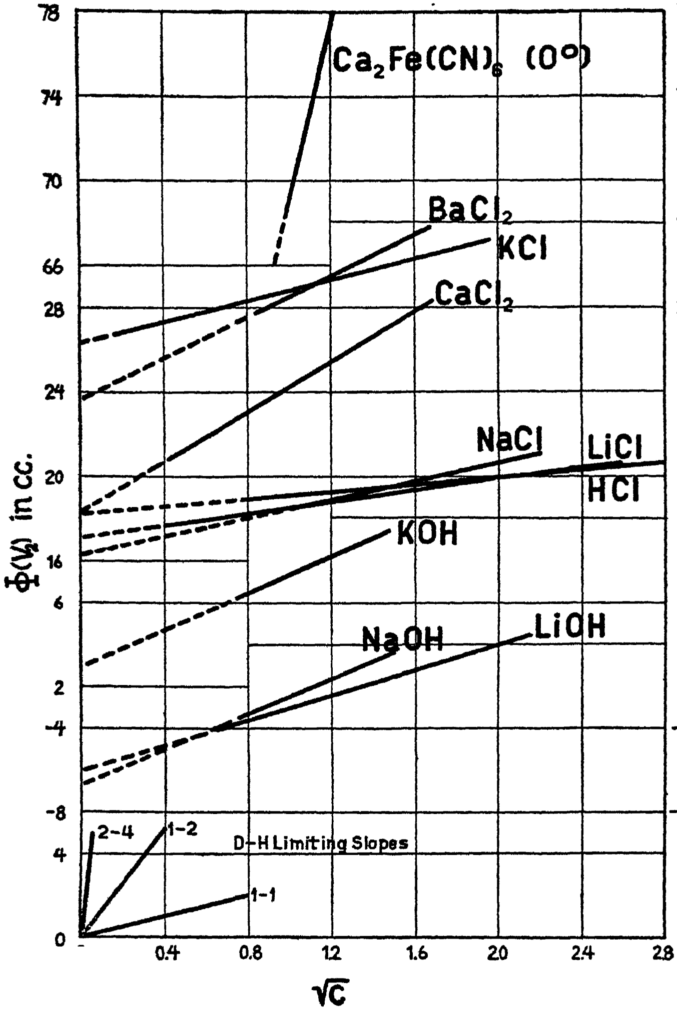

Fig. 2. Apparent Molal Volumes at 25°C.

Only a few solutes other than 1–1 electrolytes have been investigated. Geffcken (10b) includes the results for barium chloride solution, and Cantelo and Pfifer (13) give results for cobalt sulfate and cadmium iodide at 25°C. We have calculated values for the apparent molal volume of several other higher valence type electrolytes from the data in the literature. We find that the slope of these curves is markedly steeper with the higher valence ions, just as in the case of the apparent molal heat capacity curves. These general characteristics are shown by the typical lines plotted in figure 2.

APPARENT MOLAL COMPRESSIBILITIES

Recently we have studied the coefficient of compressibility of salt solutions from the point of view of the apparent molal compressibility. This function is defined by the equation

$$\Phi(K_2) = \beta V - \beta_1 V_1 \tag{5}$$

or

$$\Phi(K_2) = \beta \frac{1000}{c} - \frac{\beta_1}{d_1}\left[\frac{1000d}{c} - M_2\right] \tag{6}$$

where $\beta = -\frac{1}{V}\left(\frac{\partial V}{\partial P}\right)_T$ and β_1 are the coefficients of compressibility of solution and water, and V and V_1 have the same meaning as in equation 2. A review (14) of the rather meager data in the literature shows that $\Phi(K_2)$ is also a linear function of $c^{\frac{1}{2}}$ over a very wide range of concentration and temperature. We have recently learned that Scott (15) has independently reached conclusions very similar to our own. He has just completed an experimental study of the compressibility of the alkali halides. This will be the most complete set of data on the compressibility of salt solutions, and its publication (16) should greatly broaden our knowledge of the compressibility of solutions and should be very valuable for solution theory.

Our own study shows that the values of the apparent molal compressibility are *negative* for electrolytes. Now it can be shown that from our definition

$$\Phi(K_2) = -\frac{\partial \Phi(V_2)}{\partial P} \tag{7}$$

and if the apparent molal compressibility is negative the apparent molal volume must *increase* with pressure. This fact, which is as striking as the negative value of $\Phi(C_{p_2})$, has been noted by several investigators (17, 18). Adams found that, except in the most concentrated solutions, the partial molal volume of sodium chloride *increases* with pressure up to about ten thousand atmospheres.

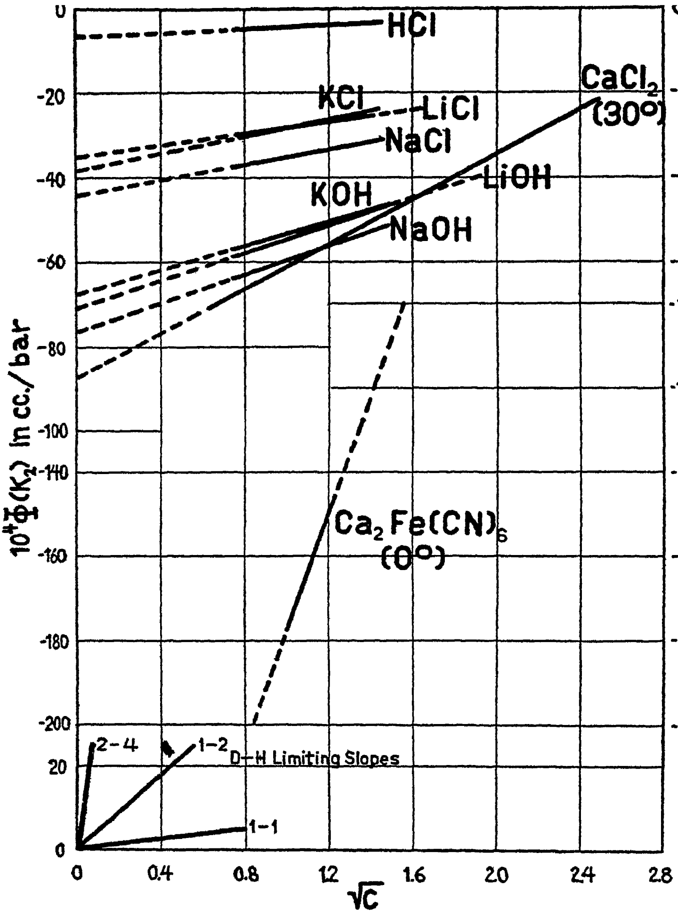

FIG. 3. APPARENT MOLAL COMPRESSIBILITIES AT 25°C.

Most of the discussion of apparent molal compressibilities in the present paper is based upon experimental data obtained by Dr. B. J. Mair and Miss Edith Lanman at Bryn Mawr College four years ago. This work will appear shortly in the Journal of the American Chemical Society. We are very grateful to these authors for their kind permission to make use of the data at the present time.

A comparison of the extrapolated values shows that the apparent ionic compressibility is also additive at infinite dilution. Once more the higher valence electrolytes show progressively steeper slopes, as can be seen in figure 3.

THEORETICAL INTERPRETATION OF THE RESULTS

A completely satisfactory theory of electrolytic solutions must account for the results which we have discussed as well as the activity and conductivity of such solutions. There are really two problems involved. First, we must explain the widely different values for the apparent molal properties at infinite dilution; the fact that the apparent molal volume increases with pressure and that the apparent molal heat capacity is negative in most strong electrolytes. Second, we must explain why all of these apparent molal properties are linear functions of the square root of the concentration; why the slope is characteristic of a particular solute and so distinctly different for different valence types. An encouraging start has been made in the theoretical treatment, although we are still very far from a complete solution of the problem.

Many years ago Tammann (19) advanced the stimulating hypothesis that an internal pressure (Binnendrucke) existed in solutions. The properties of the solution were, therefore, those of water under high pressure. This hypothesis explains qualitatively many observed facts. More recently several attempts have been made to calculate the electrostrictive force exerted by the ions upon the water molecules and thus to calculate quantitatively the properties of electrolytic solutions. Probably the most complete theoretical treatment is that of F. Zwicky (20) who has calculated the heat capacity and, more recently with Evjen (21), the compressibility and expansion of such solutions.

They start with a general expression, derived by Dällenbach, for the force exerted on an isotropic dielectric medium in which the electric field, charge density, and polarization are known from point to point. They combine this with the well-known expression for potential derived by Debye and Hückel:

$$\psi = \frac{\nu\epsilon}{D} \cdot \frac{e^{-\kappa r}}{r}$$

Thus they calculate the characteristics of the field and the pressure at any distance from the ion. In a 0.1 *c* solution of a uni-univalent electrolyte the pressures are of the order of 70,000 kg. per cm.^{2} at 1 Å. from the center of the ion and fall off very rapidly to 23 kg. per cm.^{2} at 10Å. These pressures, combined with Bridgeman's data for the different properties of water under pressure, give the corresponding properties for a solution.

At present the agreement between theory and experiment is by no means quantitative, although the general electrostrictive picture seems illuminating, since it correlates these properties and predicts that the specific heat and coefficient of compressibility of electrolytes are *less* than those of water. In addition to the mathematical difficulties, the theory is handicapped because a value of $\bar{\mu}$, the average dipole moment of the water molecules in liquid water, enters into the calculations. This value must be much less than the dipole moment of water vapor, else electrical saturation would result at room temperature, but the exact value can only be inferred.

The value of the apparent molal heat capacity of a uni-univalent electrolyte calculated by the theory is -117 calories per degree, whereas the values obtained by linear extrapolation of the Φ curves illustrated in figure 1 range from -15 to -32 calories per degree for the uni-univalent electrolytes. This agreement is hardly satisfactory. The theory predicts a greater pressure around a higher valence ion, which explains the more negative value of $\Phi^0(C_{p_2})$ for barium and calcium chloride. However, Zwicky does not include a numerical value for the 2–1 electrolyte.

In Zwicky's original treatment he calculated the pressure around a *single* ion. Now as he pointed out, an oppositely charged ion tends to neutralize this pressure, so that half way between the two it must actually be zero. Only an approximate correction was made for this effect. Since reading this manuscript, he has again taken up the problem and states in a private communication that, by calculating the pressure distribution around a *pair* of ions, one positive and the other negative, he obtains for a 1–1 electrolyte the much more satisfactory value $\Phi^0 C_{p_2} = -30$ calories per degree. He will discuss this question in a letter to the Physical Review, which should throw considerable light on the problem outlined here.

Another weakness of Zwicky's theory at the present time is that it does not predict quantitatively the differences in $\Phi^0(C_{p_2})$ for different salts of the same valence type. Actually this difference is very marked, as a glance at figure 1 will show. Zwicky attributes such specific differences to the amount of chemical hydration of the individual ions.

A somewhat more satisfying suggestion is offered by Webb (22) in a discussion of the apparent molal volume of salts at infinite dilution. He considers this volume is the result of two factors: first, the actual volume of the cavity (with a radius r_0 about 1.5 times that of the ion) in the water around the individual ion; second, a decrease in the solvent volume, due to electrostriction. The ion-solvent force he finds is very sensitive to a change in r_0, increasing greatly as r_0 decreases. This idea can afford an explanation not only for the individual values of $\Phi^0(V_2)$ but also for those of $\Phi^0(C_{p_2})$. Unfortunately, a quantitative calculation of the individual apparent molal volumes requires other data which are not known at the present time.

Perhaps the most serious objection is that the electrostriction theory does not predict the simple linear relationship between the apparent molal property and $c^{\frac{1}{2}}$.[2] Strangely enough such a linear relationship can be derived quite simply from the Debye-Hückel limiting law (23) in the case of each of the three apparent molal properties discussed here. The limiting law for the difference between the partial molal free energy of an electrolyte at any concentration c and that at infinite dilution is

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[2] Zwicky states, however, that his new method of calculation also gives this linear relationship.

$$\overline{F}_2 - \overline{F}_2^0 = (\Sigma\nu_i)\, RT \ln c - \frac{A}{D^{3/2}T^{1/2}} \cdot (\Sigma\nu_i z_i^2)^{3/2} c^{1/2} \tag{8}$$

where

$$A = \left(\frac{\pi\epsilon^6 N^3}{1000k}\right)^{1/2}$$

ν_i is the number of ions per molecule of charge z_i, N is Avogadro's number, ϵ the electronic charge, k Boltzmann's constant, and D the dielectric constant of the medium; the other symbols have their usual meaning. $(\Sigma\nu_i z_i^2)^{3/2}$ is the important *valence factor.* Substituting the values in the International Critical Tables gives $A = 2.457 \times 10^{-14}$ (in C.G.S. units).

The other properties are derived from equation 8 by thermodynamic reasoning. Randall and Rossini (1) obtained the equation for the partial molal heat capacity through the thermodynamic relationship

$$\overline{C}_{p_2} - \overline{C}_{p_2}^0 = -T\frac{\partial^2}{\partial T^2}(\overline{F}_2 - \overline{F}_2^0) \tag{9}$$

In carrying out the differentiation they assumed that the concentration was independent of the temperature, which would be true only for measurements at constant volume. The Debye-Hückel equation is derived at constant volume, while the experimental measurements are made at constant pressure. Scatchard (24) discussed this discrepancy and showed that it was easily removed by including a term for the thermal expansion in the theoretical equation. The complete equation for heat capacity was derived by La Mer and Cowperthwaite (reference 4, p. 1007).

$$C_{p_2} - \overline{C}_{p_2}^{0} = 3/4\ A\ (\Sigma\nu_i z_i^2)^{3/2} \frac{f(D,V,T)}{(DT)^{3/2}}\, c^{1/2} \tag{10}$$

where

$$f(D,V,T) = 1 + 2\frac{T}{D}\frac{\partial D}{\partial T} + 5\left(\frac{T}{D}\frac{\partial D}{\partial T}\right)^2 + \frac{2T^2}{DV}\cdot\frac{\partial D}{\partial T}\cdot\frac{\partial V}{\partial T} + \frac{2}{3}\frac{T}{V}\frac{\partial V}{\partial T} + \left(\frac{T\partial V}{V\partial T}\right)^2 -$$

$$2\frac{T^2}{D}\frac{\partial^2 D}{\partial T^2} - \frac{2}{3}\frac{T^2}{V}\frac{\partial^2 V}{\partial T^2}$$

The equation of Randall and Rossini differs only in that their $f(D, T)$ omits the last three terms of La Mer and Cowperthwaite's $f(D, T, V)$. The value of $f(D, T)$ is 16 per cent higher than that of $f(D, T, V)$ at 25°C., which illustrates the importance of the thermal expansion term.

The theoretical slope evidently requires an accurate knowledge of the dielectric properties of water, which are still in considerable doubt. The values obtained by different investigators, particularly for the derivatives, may be very different. Thus Randall and Rossini, employing E. Q. Adams' exponential representation of Kockel's data for D, obtained $f(D, T) = 1.75$, while La Mer and Cowperthwaite, using the Wyman (25) formula for the dielectric constant, obtained $f(D, T) = 4.535$ and $f(D, T, V) = 3.802$. Using La Mer and Cowperthwaite's value of $f(D, T, V)$,

$$\overline{C}_{p_2} - \overline{C}_{p_2}^0 = 4.69\,(\Sigma\nu_i z_i^2)^{3/2}\,c^{1/2} \text{ calories per degree}$$

In deriving the theoretical slope of the partial molal volume curve, Redlich (26) and Rosenfeld used the thermodynamic equation

$$\overline{V}_2 - \overline{V}_2^0 = \frac{\partial}{\partial P}\,(\overline{F}_2 - \overline{F}_2^0) \tag{11}$$

Performing the indicated differentiation upon equation 8 gave them

$$\overline{V}_2 - \overline{V}_2^0 = \frac{A}{2}\,\frac{(\Sigma\nu_i z_i^2)^{3/2}}{D^{3/2}T^{1/2}}\left[\frac{3\partial D}{D\partial P} - \beta\right]c^{1/2} \tag{12}$$

Using the pressure coefficient determined by Falkenberg (27)

$$\frac{1}{D}\frac{\Delta D}{\Delta P} = 46 \times 10^{-6} \text{ (at 16.3°C.)}$$

and the value

$$\beta = 49.2 \times 10^{-6}$$

they find

$$\frac{3}{D}\frac{\Delta D}{\Delta P} - \beta = 89 \times 10^{-6}$$

and

$$\overline{V}_2 - \overline{V}_2^0 = 0.96\ (\Sigma\nu_iz_i^2)^{3/2}\ c^{1/2}$$

More recently S. Kyropolous (28) has studied the dielectric constant of water under pressure at 20°C. We find that his values for D at 1, 500, and 1000 kg. per cm.^{2} give the equation

$$D = 80.79 + 4.80 \times 10^{-3}P - 3.11 \times 10^{-7}P^2 \tag{13}$$

where P is expressed in *bars*.[3] The corresponding value for $\frac{1}{D}\frac{\partial D}{\partial P} = 59.4 \times 10^{-6}$ bars $^{-1}$. His value at atmospheric pressure is 0.5 per cent above that calculated from Wyman's formula (80.36). The equation for the volume of water under pressure at 20°C. we calculated from Bridgeman's data (31) at 0, 500, and 1000 atmospheres.

$$V = 1.0016 - 44.5 \times 10^{-6}P + 5.25 \times 10^{-9}P^2 \tag{14}$$

where P is in bars, whence $\beta = 44.4 \times 10^{-6}$ bars^{-1}. Based on the most recent experimental data, we therefore find at 20°C.

$$\left[\frac{3}{D}\cdot\frac{\partial D}{\partial P} - \beta\right] = 134 \times 10^{-6}\ \text{bars}^{-}$$

and

$$\overline{V}_2 - \overline{V}_2^0 = 1.34\ (\Sigma\nu_iz_i^2)^{3/2}\ c^{1/2}\ \text{cc.}$$

In the course of our study of the partial molal compressibility, we derived an equation for the slope of this curve, which is here published for the first time. Differentiating equation 8 twice with respect to P gives

$$\frac{\partial^2}{\partial P^2}(\overline{F}_2 - \overline{F}_2^0) = \frac{\partial}{\partial P}(\overline{V}_2 - \overline{V}_2^0) = -\ (\overline{K}_2 - \overline{K}_2^0) \tag{15}$$

where $\overline{K}_2$ represents the partial molal compressibility. The procedure yields

$$\overline{K}_2 - \overline{K}_2^0 = \frac{A}{4}(\Sigma\nu_iz_i^2)^{3/2} f(D,P,V)\ c^{1/2} \tag{16}$$

---

[3] 1 bar = 10^{-6} dynes per cm.^{2} = 1.0197 kg. per cm.^{2} = 0.9869 atmosphere.

where

$$f(D,P,V) = \beta^2 + 2\frac{\partial\beta}{\partial P} - 6\frac{\beta}{D}\frac{\partial D}{\partial P} + 15\left(\frac{1}{D}\frac{\partial D}{\partial P}\right)^2 - \frac{6}{D}\frac{\partial^2 D}{\partial P^2}$$

Computing the numerical values for the additional differential coefficients from equations 13 and 14,

$$\frac{\partial\beta}{\partial P} = -1.03 \times 10^{-8} \quad \text{and} \quad \frac{\partial^2 D}{\partial P^2} = -62.2 \times 10^{-8}$$

whence

$$f(D,P,V) = 6.49 \times 10^{-14} \text{ cm.}^2 \text{ dynes}^{-1} \text{ bars}^{-1}$$

and

$$\overline{K}_2 - \overline{K}_2^0 = 3.23 \times 10^{-4} (\Sigma\nu_i z_i^2)^{3/2} c^{1/2} \text{ cc. per bar}$$

All the terms except the first are of about the same size and, because of the uncertainty, particularly of the second pressure coefficients, the numerical value of $f(D, P, V)$ must be rather tentative.

TABLE 1

Theoretical slopes for different valence types

VALENCE TYPE	$(\Sigma\nu_i z_i^2)^{3/2}$	THEORETICAL SLOPES		
		$\overline{V}_2$ (20°)	$10^4\overline{K}_2$ (20°)	$\overline{C}_{p_2}$ (25°)
1–1	2.828	3 8	9.1	13.2
2–1	14.69	19.7	47.5	67.8
2–4	117.6	158	380	551

We have shown how the slopes for the different partial molal quantities have been derived. In table 1 we have summarized the valence factors and also the limiting slopes for salts for different types. Those for $\overline{V}_2$ and $\overline{K}_2$ refer strictly to 20°C. and that for $\overline{C}_{p_2}$ to 25°C., but the uncertainty in the calculated value of the first two properties makes this difference negligible. The slopes for the corresponding *apparent* molal quantities are now very easily computed through the relationship

$$\frac{\partial\overline{G}_2}{\partial c^{1/2}} \cdot \frac{3}{2}\frac{\partial\Phi(G)}{\partial c^{1/2}} \tag{17}$$

which holds in dilute solution (10b).

Table 2 gives the experimental values for the apparent molal properties at infinite dilution and also for the slopes obtained by passing the best straight lines through the experimental points plotted against $c^{\frac{1}{2}}$. Only a few points for $\Phi(V_2)$ in concentrated solution were disregarded in this procedure. The theoretical Φ slopes for the different valence types are also included. This table shows that, for all three properties, the *actual* slopes are of the predicted magnitude and change with valence type in about the way that is predicted by the theory. However, there is often

TABLE 2

Experimental values for Φ^0 and $\partial\Phi/\partial c^{1/2}$ for ten solutes at 25°C.*

SOLUTE	Φ^0			$\partial\Phi/\partial c^{1/2}$		
	V_2	-10^4K_2	$-C_{p_2}$	$\Phi(V_2)$	$10^4\Phi(K_2)$	$\Phi(C_{p_2})$
1–1 (theory)	—	—	—	2.5	6.1	8.8
HCl	18.20	6.6	(29 20)	0.83	2.3	5 10
LiCl	17.06	36.4	15.63	1.42	7.5	5.31
NaCl	16.28	44 2	23 30	2.22	9.1	*13.95*
KCl	26.36	38 3	28.50	2.41	9.9	10.56
LiOH	−6 0	67.8	19.98	3 00	14 2	12.53
NaOH	−6.7	76.7	26 59	4.18	*17.0*	*17.49*
KOH	2.9	71 0	(32.10)	4.35	16 1	13.32
2–1 (theory)	—	—	—	13.1	31.6	45
$BaCl_2$	23.60	—	73.0	4.83	—	35.0
$CaCl_2$	18 25	87.4†	*66.0*	5.99	26†	25.8
2–4 (theory)	—	—	—	105	260	368
$Ca_2Fe(CN)_6$(0°C.)	25.3	316	—	43.4	139	—

* Sources: The values of $\Phi(V_2)$ are in cc. Those for HCl, LiCl, NaCl, KCl, and $BaCl_2$ are taken from Geffcken (10b); the others are calculated from density data; $Ca_2Fe(CN)_6$, from that of Berkeley and Burton (30); $CaCl_2$ and LiOH from the International Critical Tables, and NaOH and KOH from Mair and Lanman.

The values of $\Phi(K_2)$ are in cc. per bar. All are taken from Mair and Lanman except for $CaCl_2$ and $Ca_2Fe(CN)_6$ which are from Perman and Urry (29) and Berkeley and Burton (30), respectively.

The values for $\Phi(C_{p_2})$ are in 25°-calorie units. Those for NaCl and KCl are from Randall and Rossini (1), those for HCl, LiCl, LiOH, NaOH, and KOH from Gucker and Schminke (3), and those for $CaCl_2$ and $BaCl_2$ from Richards and Dole (32).

† Values at 30°C.

as much difference between two electrolytes of the same type as between two of different valence types and the slopes of the few high valence type electrolytes are noticeably *less steep* than the theory demands.

One striking regularity is apparent. When the solutes are arranged in the order of the increasing slope of the apparent molal volume curve, the slopes of the other two properties follow the same order in almost every case. Of the 1–1 electrolytes only the three slopes in italics are exceptions. The difference in the slope for ions of the same type is due to some factor that our theory does not explain but which affects all the slopes in approximately the same way. Even if subsequent investigation shows that the lines for the same type all approach a common slope at zero concentration, as Redlich and Rosenfeld postulate in the case of apparent molal volumes, our tabulation shows that the order of deviation at high concentration is essentially the same for all three properties.

TABLE 3

Non-electrolytes at 30°C.

Urea	$\Phi(V_2) = 44.3 + 0.4\, c^{1/2}$ cc.
	$10^4\Phi(K_2) = -0.5 + 2.4\, c^{1/2}$ cc. per atmosphere
Sucrose	$\Phi(V_2) = 210.6 + 3.4\, c^{1/2}$ cc.
	$10^4\Phi(K_2) = -26.8 + 24.0\, c^{1/2}$ cc. per atmosphere

Apparent molal properties of non-electrolytes

The observed linear relationship between the apparent molal properties of electrolytes and $c^{\frac{1}{2}}$ originates, according to the Debye-Hückel Theory, in the *ion atmosphere* which exists in such solutions. We might therefore expect that the apparent molal properties of non-electrolytes would show no such linear change with $c^{\frac{1}{2}}$. This is certainly true of some properties. In a study of the viscosity of solutions, Jones and Talley (33) showed that electrolytes differ from non-electrolytes in that the relative viscosity function of the former contains the square-root term, while that of the latter does not. No comprehensive study of our apparent molal properties of non-electrolytes has been made, but these substances are often assumed to behave in a "normal" way in solution. Thus Zwicky (20a) considered the apparent molal heat capacity of non-electrolytes is independent of concentration. So far we have studied only two non-electrolytes, but the implications of these results are far-reaching and may greatly

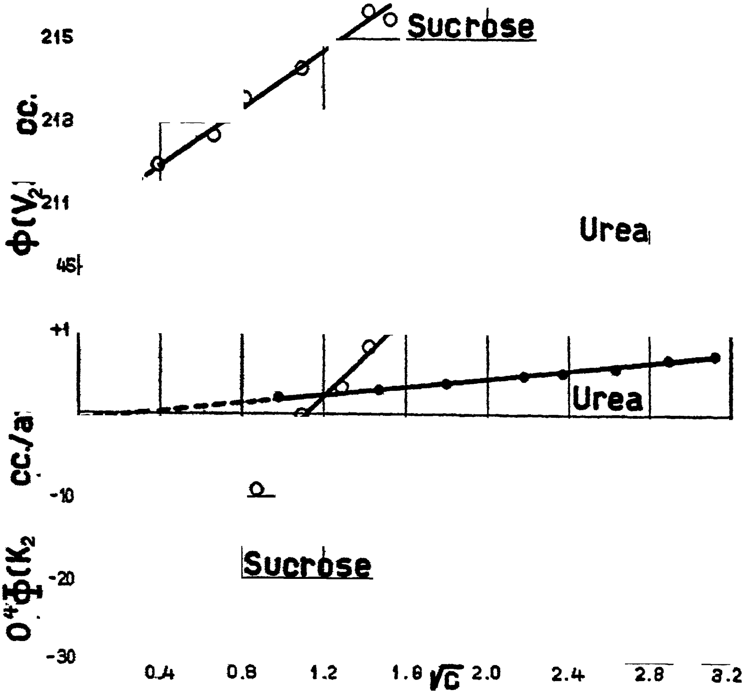

FIG. 4. APPARENT MOLAL VOLUMES AND COMPRESSIBILITIES OF NON-ELECTROLYTES.

affect our solution theory. Calculations from the data of Perman and Urry (29) show that the apparent molal volumes and compressibilities of sucrose and urea are linear functions of $c^{\frac{1}{2}}$ over the entire experimental range. For urea, the slope is small but the linear relationship holds from about 1 to 10 *c*. For sucrose, the slopes are much steeper—about those found for 2–1 electrolytes—and the linear relationship holds from 0.1 to 2.3 *c*. The equations for these properties are given in table 3, and the results are plotted in figure 4. The individual experimental points are shown, since these calculations have not been published before. They fit the linear relationship in every case within the experimental error. Unfortunately we do not know the apparent molal heat capacities of these solutes, but the slopes of the other two properties parallel each other exactly like those of the electrolytes.

If, in the case of other non-electrolytes, the square-root term appears just as it does with electrolytes, we must explain it by some other picture than that of the ion atmosphere. Are we then justified in trying to explain all of the apparent molal properties of electrolytes as due to the ion atmosphere? How much of the individuality of the lines for different ions of the same type may be due to ion-solvent forces such as exist in non-electrolyte solutions? The only answer to these questions lies in a comprehensive study of solutions of non-electrolytes, which may perhaps give us a picture of a "normal" solution, upon which the interionic forces are superimposed in solutions of electrolytes. Such an investigation will be carried out in this laboratory in the near future. A concerted attack upon solutions of non-electrolytes should lay the foundation for a more unified and consistent solution theory.

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RELATIVE ACID STRENGTHS IN ACETONITRILE

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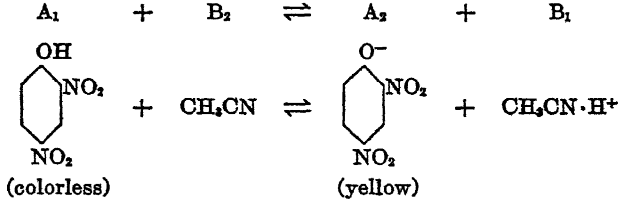
Acetonitrile, as Hantzsch (1) has shown, is a weakly basic solvent. When an acid is dissolved in acetonitrile there is established a double acid–base equilibrium; for hydrochloric acid, for example,

$$\begin{array}{ccccccc} A_1 & + & B_2 & \rightleftharpoons & A_2 & + & B_1 \\ HCl & + & CH_3CN & \rightleftharpoons & CH_3CN\cdot H^+ & + & Cl^- \end{array}$$

If the acid A_1 is an indicator, the equilibrium constant can be determined directly by the colorimetric method. We determined colorimetrically the equilibrium constants of a number of indicator acids, preparing the complete acid and basic forms of the indicator in acetonitrile by the addition of small amounts of suitable acid or base. In the case of α-dinitrophenol, for instance,

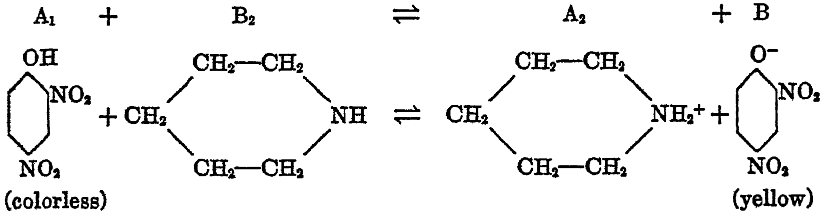


and

$$K = [CH_3CN\cdot H^+]\,[\alpha\text{-dinitrophenolate}]/[\alpha\text{-dinitrophenol}]$$

where the brackets indicate concentrations. With brom phenol blue two color changes were observed,—colorless-yellow and yellow-blue. Only the second is found in aqueous solution.

Knowing the constant for the equilibrium between the solvent and the indicator acid, it is possible to obtain the constant for the equilibrium between the indicator acid and a suitable base. Thus the constant for the equilibrium between α-dinitrophenol and piperidine



was obtained from the stoichiometric relationships, the colorimeter reading, and the constant

$$K = [CH_3CN \cdot H^+][\alpha\text{-dinitrophenolate}]/[\alpha\text{-dinitrophenol}]$$

due correction being made for the basicity of the solvent.

Knowing the constant for the equilibrium between the base and the indicator acid, it is possible to obtain the constant for the equilibrium between the base and a second acid, not an indicator, present in the solution. For example, the constant for the equilibrium between mandelic acid and piperidine

$$\begin{array}{ccccccc} A_1 & + & B_2 & \rightleftharpoons & A_2 & + & B_1 \\ C_6H_5CHOHCOOH & + & C_5H_{10}NH & \rightleftharpoons & C_5H_{10}NH_2^+ & + & C_6H_5CHOHCOO^- \end{array}$$

was obtained from the stoichiometric relationships, the colorimeter reading giving the ratio [α-dinitrophenolate]/[α-dinitrophenol], and the constant

$$K = \frac{[\alpha\text{-dinitrophenolate}][\text{piperidinium ion}]}{[\alpha\text{-dinitrophenol}][\text{piperidine}]}$$

The determination of the constants for the equilibria between acids and basic indicators was carried out in a similar way. In the case of dimethyl yellow it was not possible to get quantitative results because of the fading of the red color of the indicator. Similar chemical difficulties were encountered with other indicators in the presence of trichloroacetic acid.

In all, some forty equilibrium constants were determined. The electrolyte concentration in the experiments ranges from $\mu = 1 \times 10^{-6}$ to 1×10^{-3}. No correction was made for salt effect, and furthermore it was assumed that at these concentrations association was negligible.

The important question of a general scale of acidity has been discussed by Brönsted (2) and by others (3, 4, 5, 6) and the fundamental difficulties have been pointed out in connection with the impossibility of obtaining ionic free energies (7). For this reason the logical definition of acid strength

$$K_A = a_{H^+}c_B/c_A$$

cannot be used from solvent to solvent without arbitrary assumptions. It has been shown, however, that in constant medium relative acid strengths can be found in reference to some suitable acid–base system (2). Although an acid is defined by the equation

$$A \rightleftharpoons B + H^+$$

$$K'_A = [B][H^+]/[A]$$

the acid strength of A cannot be expressed by the equilibrium constant of the process above. This constant can, however, be related to the equilibrium constant K_0 which defines the acid property of the system having the solvent as the conjugate base

$$K_0 = [CH_3CN][H^+]/[CH_3CN \cdot H^+]$$

Dividing K_A' by K_0 one obtains

$$K_A'/K_0 = [B][CH_3CN \cdot H^+]/[A][CH_3CN]$$

the ratio being equal to the equilibrium constant for the double acid–base equilibrium. Considering the concentration of solvent as constant and transposing it to the other side, one has

$$K = K_A'[CH_3CN]/K_0 = [B][CH_3CN \cdot H^+]/[A]$$

where K is the customary dissociation constant of the acid A. The dissociation constant may therefore be taken as a measure of the acid strength in any given solvent. For solvents which are aprotic, like benzene, it is not possible to refer to the acid of which the solvent is the conjugate base. Brönsted has pointed out that in such cases one may arbitrarily choose as standard some suitable acid–base system.

Even when work is confined to one solvent the medium is changed upon the addition of solutes, so that it is impossible to work in truly constant medium. For this reason the experiments described in this paper were carried out in as dilute solution as was practicable. An alternative method would have been to maintain a medium of high and constant electrolyte concentration, employing the principle of "swamping salt" effect so successful in kinetic studies. As a general method, the latter is not so useful in non-aqueous solution, owing to the fact that many salts are insufficiently soluble, and to the fact that it is difficult to find a salt the anion or cation of which is not an acid or a base.

TABLE 1

Order of decreasing acid strength of various acids

IN ACETONITRILE	
o-Toluidinium ion	β-Naphthalenesulfonic acid
Brom phenol blue, colorless-yellow	Picric acid
β-Naphthalenesulfonic acid	Dichloroacetic acid
Picric acid	Monochloroacetic acid
Neutral red	Salicylic acid
Dichloroacetic acid	o-Chlorobenzoic acid
Salicylic acid	Mandelic acid
β-Dinitrophenol	o-Toluic acid
Brom phenol blue, yellow-blue	β-Dinitrophenol
Diphenylguanidinium ion	Glycolic acid
α-Dinitrophenol	α-Dinitrophenol
Mandelic acid	Brom phenol blue, yellow-blue
Glycolic acid	Benzoic acid
Monochloroacetic acid	o-Toluidinium ion
Piperidinium ion	Acetic acid
o-Chlorobenzoic acid	Neutral red
Isoamylammonium ion	Diphenylguanidinium ion
o-Toluic acid	Isoamylammonium ion
Benzoic acid	Piperidinium ion
Acetic acid	

Table 1 presents a list of acids arranged in order of decreasing acid strength in acetonitrile. The acid dissociation constants from which the list was made up were obtained either directly from the colorimetric measurements or by combination of equilibrium constants. For purposes of comparison, the second column of the table gives the order of decreasing acid strength for water as solvent. An examination of the table shows that the order of acid strength is not the same throughout in the two solvents. The three hydroxy-substituted carboxylic acids—salicylic, mandelic, and glycolic acids— are stronger than monochloroacetic acid in acetonitrile, whereas in water they are weaker. The influence of electric charge is shown by the greater strength

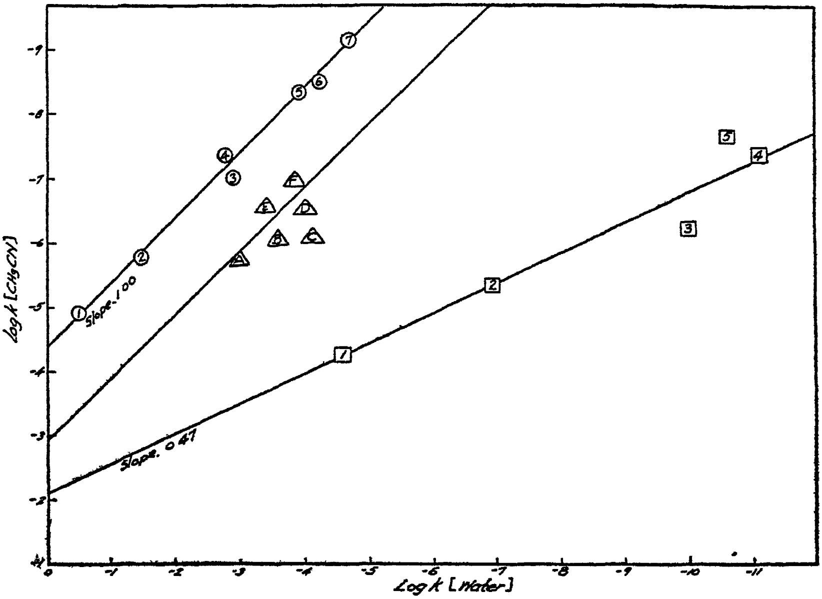


FIG. 1

1. Picric acid
2. Dichloroacetic acid
3. Monochloroacetic acid
4. *o*-Chlorobenzoic acid
5. *o*-Toluic acid
6. Benzoic acid
7. Acetic acid

△

A. Salicylic acid
B. β-Dinitrophenol
C. Brom phenol blue yellow-blue
D. α-Dinitrophenol
E. Mandelic acid
F. Glycolic acid

□

1. *o*-Toluidinium
2. Neutral Red
3. Diphenylguanidinium
4. Piperidinium
5. Isoamylammonium

of the charged acids, relative to the uncharged, in acetonitrile than in water.

In figure 1 the logarithm to the base 10 of the dissociation constant in acetonitrile is plotted against the logarithm of the dissociation constant in water. For the carboxylic acids, excluding the hydroxy-substituted acids,

$$\log K_{\mathrm{CH_3CN}} - \log K_{\mathrm{H_2O}} = -4.4$$

For salicylic, mandelic, and glycolic acids

$$\log K_{\mathrm{CH_3CN}} - \log K_{\mathrm{H_2O}} = -3$$

For the cation acids of the amine type the slope is no longer unity, the relationship being

$$\log K_{\mathrm{CH_3CN}} = 0.47 \log K_{\mathrm{H_2O}} - 2.2$$

Similar comparisons of dissociation constants have been made by Larsson (8) between alcohol and water, and by Hall (9) between acetic acid and water, and by La Mer and Downes (6) for benzene.

In connection with the quantitative estimation of acids in acetonitrile solution, acids such as perchloric acid were titrated quantitatively with diphenylguanidine using dimethyl yellow, benzoyl auramine, or thymol blue as indicator. In the case of weak acids like acetic acid, bases of sufficient strength were not available. However, Lavine and Toennies (9) have demonstrated that for mixtures of perchloric acid and acetic acid in acetonitrile it is possible to titrate quantitatively in mixed solvents using the ethylate ion as the base and thymol blue as the indicator. The first change (pink-yellow) gives the perchloric acid end-point and the second (yellow-blue) gives both.

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AN OBJECTIVE STUDY OF DILUTE AQUEOUS SOLUTIONS OF UNI-UNIVALENT ELECTROLYTES[1]

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Graphical methods of smoothing data are influenced by the personal judgment and the personal prejudices of the operator, who may emphasize either the agreement with some theory or the deviations from it. The difficulties are increased in extrapolation to zero concentration, because the measurements generally become less accurate as the concentration decreases, and because most of us draw curves which approach a linear asymptote too rapidly. An objective method, which reduces all matters of judgment to forms which can be definitely stated and systematized, is that of least squares. The results may or may not be better than those from more subjective methods, but they are always more definite.

A good body of data for the application of such a method consists of the measurements made in our laboratory of the freezing point depressions for twenty-five uni-univalent salts. All measurements below 0.1 *M* are treated; included in the tables are the three other series for uni-univalent electrolytes with a sufficient number of accurate measurements in this range. The measurements are so weighted that a deviation below 0.01 *M* of two-hundred thousandths of a degree (0.00002°C.) is equivalent to a deviation above 0.01 *M* of five hundredths of 1 per cent (0.05 per cent); that is, the function j of Lewis and Randall is given unit weight for depressions greater than 0.04°C., and weighted proportionally to the square of the ratio of the depression to 0.04°C.

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[1] Contribution No. 308 from the Research Laboratory of Physical Chemistry of the Massachusetts Institute of Technology.

for smaller depressions. Our own measurements for all the salts except the slightly soluble potassium perchlorate have approximately the same distribution. For them a systematic error of one-tenth of 1 per cent in the concentration or in the temperature would give a deviation in the A coefficient of about 2.5 per cent for equation 2 and of about 4.5 per cent for equation 3. Such an error might arise for any one salt from an error in the analysis or from impurities. An error in the temperature scale would cause the same deviation for all the salts. In a recent calibration of our thermocouples the standard deviation for forty-three measurements was 0.08 per cent, and considerable confidence is placed in the result. Coefficients have been calculated for the equations:

$$j = Am^{1/2} \tag{1}$$

$$j = Am^{1/2} + Bm \tag{2}$$

$$j = Am^{1/2} + Bm + Cm^{3/2} \tag{3}$$

$$j = Am^{1/2} + Bm + Cm^{3/2} + Dm^2 \tag{4}$$

$$j = 0\ 3738\ m^{1/2} + Bm \tag{5}$$

$$j = 0.3738\ m^{1/2} + Bm + Cm^{3/2} \tag{6}$$

$$j = 0.3738\ m^{1/2} + Bm + Cm^{3/2} + Dm^2 \tag{7}$$

Equation 1 need not be considered because the agreement with the data is poor, and equation 4 is eliminated because the agreement is only slightly better than for equation 3 while the coefficients become very large.

Table 1 shows the percentage deviation of the A coefficients from the theoretical value 0.3738 for equations 2 and 3. The difference between these deviations for the two equations is a measure of the reliability of either value. The average deviations for twenty-one alkali salts are −9 per cent for equation 2 and −3 per cent for equation 3, and half the individual deviations are less than 10 per cent. The measurements on the acids and on thallium chloride agree, probably within their accuracy. These results indicate that the limiting slope is probably not more than 10 per cent different than that calculated from the Debye theory.

To determine whether the measurements demand a slope slightly smaller than that given by the theory, the standard deviations (root-mean-square deviations) in per cent from equations

TABLE 1

Least square treatment of freezing point measurements

SALT	REFERENCE	DEVIATION OF A IN PER CENT		STANDARD DEVIATIONS IN PER CENT				
		Equation 2	Equation 3	Equation 2	Equation 3	Equation 5	Equation 6	Equation 7
LiCl	(14)	−1	+18	0.14	0.09	0.14	0.13	0.11
LiBr	(14)	−13	−4	0.08	0.06	0.23	0.07	0.07
$LiNO_3$	(11)	−10	−1	0.11	0.09	0.18	0.09	0.09
$LiClO_3$	(14)	−8	+7	0.11	0.09	0.15	0.10	0.10
$LiClO_4$	(14)	−15	−10	0.09	0.09	0.23	0.09	0.09
LiO_2CH	(14)	−7	−3	0.21	0.21	0.25	0.21	0.21
$LiO_2C_2H_3$	(14)	−8	−3	0.14	0.14	0.20	0.14	0.14
NaCl	(14)	−11	−9	0.13	0.13	0.22	0.14	0.14
NaBr	(14)	−24	−17	0.09	0.08	0.40	0.12	0.07
$NaNO_3$	(11)	−12	−6	0.07	0.06	0.20	0.07	0.06
$NaClO_3$	(14)	−8	−5	0.08	0.08	0.14	0.08	0.08
$NaClO_4$	(14)	−6	−7	0.08	0.08	0.13	0.09	0.08
NaO_2CH	(14)	−12	−12	0.13	0.13	0.25	0.15	0.14
$NaO_2C_2H_3$	(14)	−7	+10	0.13	0.11	0.20	0.11	0.11
KCl	(14)	−7	+5	0.21	0.19	0.24	0.20	0.19
KBr	(14)	−11	−10	0.07	0.07	0.19	0.09	0.07
KNO_3	(11)	−4	−21	0.10	0.08	0.11	0.10	0.06
$KClO_3$	(14)	−16	−36	0.11	0.11	0.30	0.16	0.11
$KClO_4$*	(14)	+7	+44	0.26	0.24	0.27	0.27	0.24
KO_2CH	(14)	−15	−10	0.18	0.18	0.33	0.19	0.18
$KO_2C_2H_3$	(14)	−6	+21	0.28	0.23	0.29	0.26	0.23
Average		−9	−3	0.13	0.12	0.22	0.14	0.12
NH_4Cl	(12)	+16	+45	0.21	0.08	0.34	0.29	0.17
NH_4Br	(12)	+21	+54	0.24	0.08	0.43	0.35	0.20
NH_4I	(12)	+6	+22	0.16	0.13	0.19	0.18	0.15
NH_4NO_3	(12)	+14	+35	0.17	0.11	0.27	0.23	0.16
HCl	(7)	−3	−3	0.09	0.09	0.09	0.09	0.08
HNO_3	(1)	−18	−50	0.33	0.31	0.38	0.34	0.32
TlCl†	(7)	−18	−1	0.15	0.14	0.22	0.15	—

* Maximum concentration = 0.05 *M*.

† Maximum concentration = 0.006 *M*.

2, 3, 5, 6, and 7 are given in the next columns of table 1. Except for equation 5 the standard deviations are essentially the same;

that is, if more than one constant is determined from the data, it makes little difference whether there are two or three such constants and whether one of them is proportional to the square root of the concentration or the square-root term is determined from the theory and all adjustable constants attributed to higher terms. The measurements give no indication that the limiting law is different from the theoretical limiting slope.

The results for the ammonium salts, however, differ markedly from the others. The slope obtained is much larger than the theoretical, but the difference between the deviations for the two equations may be taken as evidence that the form of the equations is not adapted to these data, and that the measurements on ammonium salts furnish no evidence either for or against the theory.

The difficulty of obtaining the initial deviation from the limiting law may be seen from the first three columns of table 2, which are the values of $-B$ from equation 5 determined from our smoothed curve at 1.0 M, 0.1 M, and 0.01 M, respectively. The last place given corresponds to 0.01, 0.001, and 0.0001 in j. Throughout this range the variation left to personal judgment is less than 0.001, so that the 1.0 M results are precise as given, the 0.1 M ones uncertain to about one unit in the second place, and the 0.01 M results uncertain to one unit in the first place. At 1.0 M, however, the spread in the individual results is small and the concentration much too great for a simple interpretation. The fact that the value of B changes so much with the concentration shows that the problem of obtaining the initial value is a difficult one, and indicates the reason for the large deviations from equation 5 in the least square treatment.

The last two columns of table 2 show the values of $-B$ from equations 6 and 7 by the least square method. The difference between these two also gives an indication of the reliability of either. If they disagree, it requires a very careful analysis to tell which is to be preferred. We cannot say that either is better than the value from the smoothed curve at 0.01 M, except that the values from least squares are entirely objective.

In the majority of cases the three do not differ greatly except for lithium chloride and the ammonium salts, for which the measurements indicate much curvature in very dilute solutions.

TABLE 2

-B coefficients

SALT	EQUATION 5 AT CONCENTRATION			LEAST SQUARES	
	1.0 *M*	0 1 *M*	0 01 *M*	Equation 6	Equation 7
LiCl	0.40	0.61	0.46	0.70	0.35
LiBr	0.43	0.70	0 97	1.01	1.09
$LiNO_3$	0.38	0.63	0.81	0.90	0.97
$LiClO_3$	0.40	0.66	0 90	0.92	0.78
$LiClO_4$	0.45	0.73	1.09	1 17	1.40
LiO_2CH	0.30	0.52	0.70	0.68	0.72
$LiO_2C_2H_3$	0.36	0.58	0.73	0.77	0.82
NaCl	0.28	0.52	0 77	0.76	0.87
NaBr	0.31	0.60	1.15	1.17	1.62
$NaNO_3$	0.18	0.38	0 63	0.68	0.87
$NaClO_3$	0.21	0.42	0.59	0.62	0.74
$NaClO_4$	0.23	0.46	0.57	0.62	0.86
NaO_2CH	0.30	0.55	0.79	0.81	1.05
$NaO_2C_2H_3$	0.38	0 66	0.86	0.85	0.62
KCl	0.25	0.45	0.59	0.64	0.60
KBr	0.25	0.47	0.65	0.72	0.94
KNO_3	0.06	0.15	0 26	0.24	1.05
$KClO_3$	—	0.22	0.66	0.73	1.49
$KClO_4$	—	—	−0.05	−0.21	−1.20
KO_2CH	0.31	0.56	0 88	0.87	1.04
$KO_2C_2H_3$	0.40	0.67	0.85	0.88	0.33
NH_4Cl	0.26	0.40	−0.37	0.18	−0.78
NH_4Br	0.26	0.40	−0 57	0.11	−0.96
NH_4I	0.27	0.46	0.07	0.40	−0.10
NH_4NO_3	0.16	0.27	−0.24	0.08	−0.70
HCl	—	—	0.76	0.76	0.68
HNO_3	0.34	0 58	0.62	1.01	2.38

Any one shows that the effect is far too complicated to be explained by a single parameter such as the mean collision diameter. The three methods together give twenty-one comparisons of the order of arrangement of the alkali salts of the seven anions studied. In order of increasing magnitude they are: K–Na–Li, 7; K–Li–Na, 4; Li–Na–K, 4; Li–K–Na, 3; Na–K–Li, 2; Na–Li–K, 1. The seven averages of the three methods for each anion give five of the six possibilities. The choice of material studied is too arbitrary to draw many conclusions other than the proof that the problem of the specific characteristics of the ions is a very complex one.

TABLE 3

Electromotive force of hydrochloric acid cells in millivolts

OBSERVER	HIGHEST CONCENTRATION	$E_0 - 222.00$				A		B		STANDARD DEVIATION			
		Equation 8	Equation 9	Equation 10	Equation 11	Equation 8	Equation 9	Equation 10	Equation 11	Equation 8	Equation 9	Equation 10	Equation 11
	M												
Carmody (2).....	0.01	0.43	0.28	*0.21*	0.22	−17	−5	*86*	89	0.08	0.07	0.08	0.08
Linhart (5)......	0.01	0.71	0.56	*0.52*	0.53	−19	−3	*105*	120	0.11	0.09	0.09	0.09
Nonhebel (6)....	0.01	0.82	0.98	*0.52*	0.65	−26	−41	*151*	403	0.14	0.12	0.16	0.14
Roberts (8)......	0.01	0.89	0.32	*0.45*	0.41	−22	7	*93*	66	0.08	0.07	0.07	0.07
Roberts (8)......	0.1		0.55		*0.37*		−7		*88*		0.09		0.09
Harned (3)......	0.1		0.67		*0.44*		−8		*89*				

The opportunity to compare the measurements of several observers with the same material is offered on the electromotive force of the cell

$$H_2, Pt, HCl\ (m), AgCl, Ag$$

Table 3 contains the data for the treatment of these results with the equations

$$E_0' = E_0 - Am^{1/2} \tag{8}$$

$$E_0' = E_0 - Am^{1/2} + Bm \tag{9}$$

$$E_0' = E_0 - 59.62\ m^{1/2} + Bm \tag{10}$$

$$E_0' = E_0 - 59.62\ m^{1/2} + Bm + Cm^{3/2} \tag{11}$$

The values are expressed in millivolts. The concentration range is from the greatest dilution to 0.01 M or to 0.1 M, both ranges being used when the distribution of measurements warrants it, and the measurements are each given unit weight.

These measurements give the same indication as the freezing points regarding the limiting law. Equation 8 leads to a slope about 20 per cent less than the theory up to 0.01, and about 40 per cent too small up to 0.1 M, but equation 9 gives a slope within a few per cent of the theoretical; equation 10 with the theoretical slope agrees practically as well as equation 9 with adjustable slope. It should be noted that these results are all carried to one place further than the experimental data of Linhart and of Carmody.

If the theoretical slope is assumed, equation 10 gives the best values of the constants in the range to 0.01 M, and equation 11 to 0.1 M. The respective values of E_0 and of B are italicized. The values of B for Carmody's, Roberts' (two ranges), and Harned and Ehlers' measurements agree very closely. Linhart's measurements lead to a slightly higher value, and Nonhebel's are seriously different. In the E_0 values Roberts and Harned and Ehlers agree closely, Carmody yields a value 0.2 millivolt lower, and Linhart and Nonhebel 0.1 millivolt higher. Probably Nonhebel's results should be given little weight on account of the large deviations; and all of Linhart's measurements except those with the second and third most dilute solutions fit very closely the curve for Roberts' measurements. There remains the discrepancy of 0.2 millivolt between the measurements of Carmody and those of other observers, which appears to be almost independent of the concentration. It is possible that it should be attributed to differences in the silver–silver chloride electrodes, but further experiments would be required to show this. Again it is not claimed that the least square results have any advantage other than that of complete objectivity over intelligent extrapolation by other methods. The E_0 obtained from Linhart's measurements lies between the values obtained by Scatchard (222.6) (9) and by Hitchcock (222.4) (4) from graphic extrapolation of the earlier measurements; that from Carmody's measurements agrees well with the value obtained by Spencer (222.2) (13); and the results from the Yale laboratory's measurements agree very well with the values (222.40 and 222.39) obtained by the observers (8, 3), and lies midway between the two results (222.35 and 222.45) obtained by Scatchard (10) from Linhart's measurements at 0.01 *M* and his own results for higher concentrations. In all these cases the agreement depends largely upon the acceptance of the theoretical limiting law.

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SURFACE CHEMISTRY[1]

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The phenomenon of adsorption has been known and has been studied for many years. For example, Sir James Dewar found that charcoal cooled in liquid air was capable of taking up very large quantities of such gases as oxygen and nitrogen. This was known to be a surface action depending on the very fine state of division of the charcoal.

The effect of soap in lowering the surface tension of water depends upon the presence of a higher concentration of soap molecules in the surface layer than in the solution.

Willard Gibbs proved thermodynamically that there is a general relation between the surface adsorption, the lowering of the surface tension, and the concentration of the solution. The equation that he deduced can readily be put in the form

$$\frac{\mathrm{d}F}{\mathrm{d}(\ln p)} \quad \sigma kT \tag{1}$$

where p is the partial pressure of the vapor of the adsorbed substance in equilibrium with the surface of the liquid, or it may be the partial osmotic pressure of a substance dissolved in the liquid, σ is the number of molecules adsorbed on the surface per unit area, T is the absolute temperature, and k is the Boltzmann constant, 1.37×10^{-16} erg deg.$^{-1}$, and F, which may be called the spreading force, is given by

$$F = \gamma_0 - \gamma \tag{2}$$

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[1] This paper was presented as the Nobel Lecture in Chemistry in Stockholm on December 14, 1932. It is designed to summarize the author's contributions and present views in this field, but does not adequately describe the work of others.

where γ_0 is the surface tension of the pure solvent (in dynes cm.$^{-1}$) and γ is the surface tension of the solution.

The form of Gibbs' equation represented by equation 1 is thermodynamically valid if the film is in equilibrium with the two volume phases and if the law of ideal gases

$$p = nkT \tag{3}$$

is applicable in the volume phases.

Prior to 1910 many different theories of adsorption had been proposed, but none of them had been very successful. In most of these theories the increased concentration of the adsorbed substance near the surface was thought to be analogous to the retention of the earth's atmosphere by the gravitational attraction of the earth. An adsorbed gas was thus regarded as a kind of miniature atmosphere extending out a short distance from a solid substance. In general such theories were called upon to account only for qualitative aspects of the adsorption of gases on solids. Most of the knowledge of adsorption was empirical. Even Gibbs' law had not been verified experimentally.

When I first began to work in 1909 in an industrial research laboratory (1, 2) I found that the high vacuum technique which had been developed in incandescent lamp factories, especially after the introduction of the tungsten filament lamp, was far more advanced than that which had been used in university laboratories. This new technique seemed to open up wonderful opportunities for the study of chemical reactions on surfaces and of the physical properties of surfaces under well-defined conditions. I resolved to try the effect of introducing very small quantities of various gases into a highly evacuated bulb containing a tungsten filament. Since by a McLeod gauge pressures as low as 10^{-8} atmospheres could be measured, it was possible to observe the disappearance of an amount of gas of less than 0.1 cubic millimeter measured at atmospheric pressures. The use of a tungsten filament presented particular advantages, for this could be heated in high vacuum to temperatures of over 3000°K., so that all impurities could readily be distilled out of the filament. The ease and accuracy with which any desired temperature could be produced and measured also was important.

When a hot body, such as a filament, is in contact with a gas at atmospheric pressure in a glass bulb, the convection currents and the uncertain temperature distribution in the gas are factors which greatly complicate any interpretation of observed phenomena involving the interaction of the filament with the gas.

If the gas, however, is at a pressure as low as 100 baryes,[2] the mean free path of the molecules is many times greater than the diameter of the ordinary tungsten filament. Each molecule which strikes the filament has thus made so many collisions with other molecules since its last collision with the filament, that the effective temperature of the gas in contact with the filament may be taken to be the same as that of the bulb. The disturbing effects of convection currents are then entirely eliminated and the rate of arrival of gas molecules at the surface of the filament can be calculated according to the laws of the kinetic theory of gases. This theory leads to the equation

$$\frac{}{(2\pi mkT)^{1/2}} \tag{4}$$

where μ is the rate of arrival of the gas molecules expressed in molecules cm.$^{-2}$ sec.$^{-1}$, and m is the mass of the molecule. By inserting numerical values this equation becomes

$$\mu = 2.65 \times 10^{19}\, p\, (MT)^{-1/2} \tag{5}$$

where M is the molecular weight of the gas (oxygen = 16) and p is expressed in baryes. By using filaments of small size and bulbs of large size, it was possible to measure experimentally such high rates of disappearance of gas (clean-up) that every molecule that struck the filament disappeared. Under usual conditions, however, the rates of clean-up were far less than this theoretical maximum. The fraction, ϵ, of all the impinging molecules which reacted on striking the filament could thus be determined.

Working in this way, a systematic study was undertaken of the effects of such gases as oxygen, hydrogen, nitrogen, carbon monoxide, and their mixtures, etc., on filaments of tungsten carbon, molybdenum and platinum. I shall refer only to those cases where the experiments have thrown light upon the phenomenon of adsorption.

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[2] A barye or C.G.S. unit of pressure, 1 dyne cm.$^{-2}$, is almost exactly 10^{-6} atmosphere.

CLEAN-UP OF HYDROGEN (3)

When a tungsten filament is heated to temperatures of 1500 °K. in hydrogen at about 20 baryes pressure, the hydrogen slowly disappears, the pressure decreasing with time as indicated in curve I of figure 1. The pressure falls to a very low value in ten to twenty minutes. If more hydrogen is introduced, the rate of clean-up is somewhat slower, the pressure decreasing according to curve II. Although analysis shows the residual gas to be pure hydrogen, the clean-up gradually comes to a standstill.

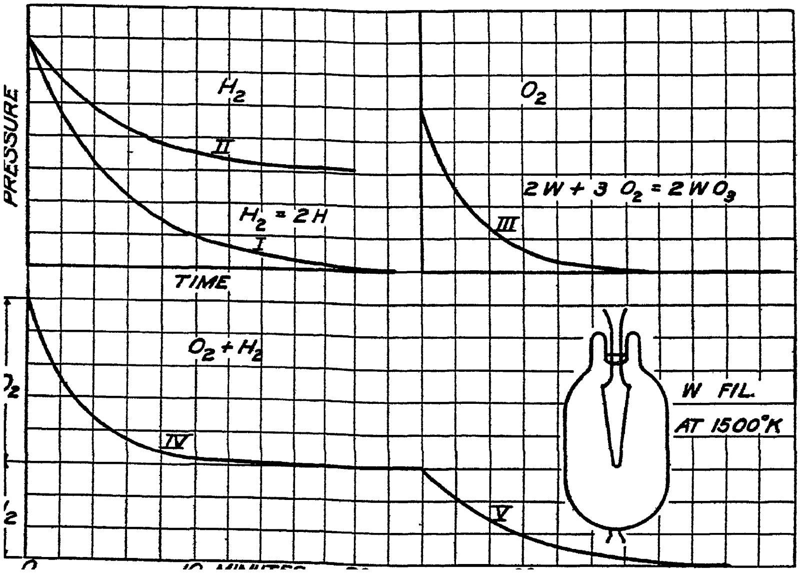

Fig. 1. Clean-up of Hydrogen and Oxygen by a Tungsten Filament

With a bulb containing two filaments, it is found that the lighting of the second filament does not cause a recovery in the rate of clean-up. This proves that the gas which disappears is not taken up by the filament itself. By keeping the bulb in liquid air, a greater total amount of clean-up is obtained. Such investigations show that the hydrogen which disappears becomes adsorbed on the surface of the bulb, but that the bulb is capable of adsorbing only a limited amount of hydrogen. This hydrogen adsorbed on the glass is capable of reacting with oxygen at room temperature after the filament has been allowed to cool. The adsorbed hydrogen is therefore in a chemically very active state. It was finally proved that the heated tungsten filament dissociates (4, 5, 6, 7, 8) a small fraction of the incident hydrogen molecules into atoms, and that these atoms, because of their unsaturated chemical nature, exhibit a strong tendency to be adsorbed on glass. These hydrogen atoms, however, are capable of reacting with one another and forming molecules. From this point of view, it should be impossible to hold on the glass more hydrogen than could form a layer one atom deep.

By cooling the bulb in liquid air the adsorption increased. The maximum amount of hydrogen adsorbed on the glass in these experiments was 0.03 mm.^{3} per cm.^{2} measured as molecular hydrogen at atmospheric pressure. This corresponds to $\sigma = 1.15 \times 10^{15}$ atoms of hydrogen per cm.^{2} which is equal to the number of spheres of diameter[3] 2.8 A.U. which can be packed per cm.^{2} into a close-packed hexagonal lattice. The spacing of the adsorbed atoms is probably determined by the arrangement of the atoms in the underlying glass which provide "elementary spaces" in which atoms can be held. If the average diameter of the atoms of the glass can be assumed to be 2.8 A.U., the observed maximum amount of adsorbed hydrogen thus agrees well with that to be expected in a monatomic film. If a glass surface saturated with atomic hydrogen at liquid air temperature is allowed to warm up to room temperature, part of the hydrogen escapes as molecular hydrogen; the rest can be driven off at 300°C. Since adsorbed hydrogen atoms probably react on contact to form molecular hydrogen, then experiments indicate that the surface mobility of the adatoms[4] is very small at room temperature.

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[3] Atomic and molecular distances will be given in terms of the Ångström unit, 10^{-8} cm., which will hereafter be denoted by A.U.

[4] J. A. Becker (Trans. Am. Electrochem. Soc. **55**, 153 (1929)) has suggested this term for adsorbed atoms.

It was shown that the atomic hydrogen can diffuse long distances through glass tubing at room temperature (but not at liquid air temperature) and can then reduce metallic oxides (9) such as WO_3, CuO, Fe_2O_3, ZnO, or PtO_2, and can dissolve in platinum sufficiently to raise its resistance (10). It reacts at room temperature with phosphorus (3) to form PH_3.

OXYGEN FILMS ON TUNGSTEN

When a tungsten filament is heated to 1500°K. or more in oxygen at very low pressures, such as 100 baryes or less, the oxygen reacts (11) with the tungsten to form the oxide WO_3, which evaporates from the filament at these temperatures as fast as it is produced, leaving the surface of the filament apparently clean. At temperatures below about 2200°K. the presence of extremely small amounts of oxygen (10^{-6} mm.) decreases the electron emission from a tungsten filament to values that range from 10^{-2} to 10^{-5} of that from pure tungsten, depending on the temperature at which the emission is measured. This modification of the properties of the surface must depend upon the presence of a film which contains oxygen. When the filament temperature is high, such as 2000°K. or more, the emission returns to a normal tungsten emission as soon as the oxygen is completely consumed or is removed by vaporizing into the bulb a "getter" such as magnesium. If, however, the filament temperature is as low as 1500°K., complete removal of oxygen from the gas phase even by introducing cesium vapor as a getter, does not remove the oxygen film on the tungsten surface after it has once been formed. This means that the oxygen from such a film does not evaporate appreciably at 1500°K. Measurements at higher temperatures show that about half of the adsorbed oxygen evaporates in 27 minutes time at 1860°K. and in about twenty seconds at 2070°K. (12). From the temperature coefficient at this rate of evaporation it can be concluded that it will take about three years at 1500°K. to remove half the film by evaporation and that the heat of evaporation is of the order of 160 kg.-cal. per gram atom.

This heat of evaporation is far greater than the heat of dissociation of oxygen into atoms, so we have very direct evidence that the forces that hold oxygen to a tungsten surface are comparable to the most powerful chemical forces known. This gives reason for believing that the oxygen film which so greatly decreases the electron emission from tungsten consists of a single layer of oxygen atoms which are chemically combined with the underlying tungsten atoms.

The electron emission from the tungsten filament in the presence of oxygen at temperatures below 1800°K. is found to be independent of the pressure of oxygen provided that more than about 10^{-3} barye is present. This must mean that the surface is practically completely covered with oxygen and that an increase in oxygen pressure does not cause the thickness of the layer to increase beyond that of a single layer of atoms.

Curve III in figure 1 indicates the way in which the pressure of oxygen in the bulb decreases with time when the tungsten filament is maintained at 1500°K. The rate of disappearance of the oxygen is proportional to the oxygen pressure and there is no fatigue effect, such as was observed during the clean-up of hydrogen.

INTERACTION OF OXYGEN WITH HYDROGEN IN CONTACT WITH TUNGSTEN FILAMENT

Mixtures of oxygen and hydrogen at low pressures in a bulb containing a tungsten filament behave in an extraordinary manner (see reference 13, p. 2271; reference 14; and reference 15, p. 608). Typical results obtained with a filament temperature of 1500°K. are shown in curves IV and V of figure 1. These curves were obtained with a mixture of three parts of hydrogen and five parts of oxygen. When the filament was lighted, the gas disappeared at exactly the same rate as shown in curve III when five parts of oxygen alone were present. After about fourteen minutes practically all of the oxygen had disappeared. This was confirmed by analysis of the residual gas which was found to be pure hydrogen. This hydrogen, however, did not dissociate in the usual way into atoms and disappear by adsorption on the glass walls as shown in curve I, but the pressure remained practically constant until after about twenty-four minutes when the pressure suddenly began to decrease as indicated by curve V.

This curve V is, however, identical with curve I, which is characteristic of the clean-up of hydrogen in absence of oxygen. Repeated experiments with different amounts of oxygen and hydrogen prove that hydrogen does not interfere with the clean-up of oxygen but that a minute trace of oxygen of about 10^{-8} barye completely prevents the dissociation of hydrogen into atoms by a tungsten filament at 1500°K. The oxygen thus acts as a catalytic poison. Experiments of this kind can be used to make quite accurate chemical analyses of mixtures of oxygen and hydrogen.

The fact that a monatomic film of oxygen on tungsten does not react with hydrogen at 1500°K. is a striking indication that the oxygen is in a condition far different from that of gaseous oxygen. The results, however, confirm our conclusion that the film consists of oxygen atoms which are chemically saturated with the tungsten atoms with which they are in contact.

In view of the fact that an oxygen film on tungsten at 1500°K. does not evaporate in less than a year, it is remarkable that in the presence of hydrogen the beginning of the hydrogen clean-up (curve V) is so sharp. Since curve V is exactly like the lower part of curve I, it appears that once the hydrogen begins to dissociate, the oxygen is suddenly completely removed from the surface; in other words, hydrogen can remove monatomic oxygen films from the tungsten surface if the amount of oxygen on the surface is less than a definite amount. This probably means that the adsorbed oxygen molecules cannot react with hydrogen atoms directly but can react with hydrogen atoms adsorbed in adjacent spaces on the tungsten surface.

THORIUM ON TUNGSTEN (16)

When a tungsten filament which is made from tungstic oxide containing about 1 per cent of thoria, ThO_2, is heated to temperatures of 2800°K. or more, a minute fraction of the thoria is reduced to metallic thorium. The thoria exists in the filament in the form of minute spherical particles distributed throughout the tungsten crystals and not at the boundaries of crystals. If the filament is then heated for a period of a few minutes at 1900° to 2000°K., the metallic thorium which has been produced at the higher temperatures diffuses slowly through the crystal grains to the crystal boundaries, and then diffuses rapidly along these boundaries to the surface of the filament, and then spreads over the surface of the filament by surface migration and forms a monatomic film of adsorbed thorium atoms on the surface of the filament. At 2000°K. the rate of evaporation of thorium from the filament is so small that sufficient thorium soon accumulates on the filament to form a nearly complete monatomic film. If the temperature is raised to 2200°K. or 2400°K., the rate of evaporation of the thorium from the surface increases so much more rapidly than the rate of arrival from the interior by diffusion, that the actual surface concentration decreases greatly.

These changes in the thorium content of the adsorbed film can be studied by measurements of the electron emission from the filament at a standard low temperature, called the testing temperature, which is chosen so low that neither diffusion to the surface, nor evaporation from the surface, causes appreciable changes in the adsorbed film. A convenient testing temperature is 1500°K. At this temperature the presence of adsorbed thorium on the surface may increase the electron emission as much as 10^5-fold over that from a pure tungsten surface.

Such experiments make it possible to investigate the electrical properties of surface films having known amounts of thorium. On the assumption that each thorium atom on the surface acts as a dipole having a definite dipole moment, it is possible to show that the logarithm of the electron emission should increase linearly with the number of thorium atoms on the surface. The experiments showed that for low concentrations of thorium this relation holds approximately.

There are several indications that the adsorbed film of thorium that is formed by diffusion from the interior never exceeds one atom in thickness.

THE INTERACTION OF CARBON DIOXIDE WITH CARBON FILAMENTS

If a carbon filament is heated to a temperature above 1700°K. in the presence of carbon dioxide at low pressure, one molecule of carbon monoxide is liberated from every molecule of carbon dioxide (see reference 2, p. 1154). If this carbon monoxide is pumped out from the bulb and the filament is then heated to 2300°K., a volume of carbon monoxide is slowly liberated equal to that originally formed from the dioxide. This proves that each carbon dioxide molecule which comes in contact with the filament and reacts loses one oxygen atom to the filament and thus produces a carbon monoxide molecule. The oxygen atoms thus transferred to the filament form a monatomic film of oxygen atoms covering the surface, these atoms being chemically combined with the carbon atoms with which they are in contact, presumably by double bonds. This adsorbed film on the filament is very stable at 1700°K., but when heated to 2300°K., the film is destroyed, not by the evaporation of the oxygen atoms, but by the breaking of the bonds between the carbon atoms which are attached to the oxygen and the underlying carbon atoms with which they are in contact. Thus the oxygen escapes as carbon monoxide.

From this point of view we see that we can look upon the adsorbed film on the carbon filament either as consisting of adsorbed oxygen, or as an adsorbed film of oriented carbon monoxide molecules, or carbonyl radicals which are chemically attached by their carbon atoms to the underlying carbon atoms in the filament. It is to be expected that the properties of the adsorbed film would be very different if it consisted of carbon monoxide molecules attached to the underlying surface through their oxygen atoms. These experiments thus led to the concept that the properties of adsorbed films should in general depend on the orientation of the molecules or radicals in the film. It seemed to the writer (in 1915) that evidence of such orientation could be found among the data on the surface tensions of pure liquids.

SURFACE ENERGIES OF PURE LIQUIDS (17, 18)

If a prism of liquid having a cross section of 1 sq. cm. is divided into two parts by an imaginary plane perpendicular to the axis of the prism, and the two portions of the liquids are then separated, there has been an increase in the surface of the liquid of 2 sq. cm. The total energy theoretically required per square centimeter of new surface to bring about this separation may be called the total surface energy γ_0. This is related to the free surface energy γ, which is equivalent to the surface tension of the liquid, by the relation

$$\gamma_0 \quad \gamma - T\frac{d\gamma}{dT}$$

By measurements of the surface tension, the surface energy γ_0 can thus be measured. This quantity represents the potential energy of the molecules which form the surface of the liquid (per square centimeter) in excess of that which the same molecules possess when they are in the interior of the liquid.

TABLE 1

Surface properties of molecules

SUBSTANCE	V VOLUME	S SURFACE	T_B BOILING POINT	λ HEAT OF EVAPORATION	λ/S	γ_0
	A.U.^{3}	A.U.^{2}	°K.	erg × 10^{-14}	erg cm.$^{-2}$	erg cm.$^{-2}$
He	52.	68.	4.3	0.24	0.35	0.59
H—H	47.	63.	20.5	1.67	2.7	5.4
H—OH	30.	48.	373.	67.	140.	118.
A	47.	63.	88.	11.3	18.	35.3
CH_4	64.	78.	112.	16.3	21.	—
n-C_8H_{18}	266.	200.	398.	56.	28.	50.7
n-$C_8H_{17}OH$	260.	198.	467.	82.	41.5	50.7

In table 1 data are given for a few substances which serve to illustrate the interrelation (19, 20) between the orientations of molecules and other properties of liquids. The latent heat of evaporation, λ, which, according to Trouton's rule, is approximately proportional to the absolute boiling point, T_B, serves as a measure of the energy needed to bring a molecule from the interior of the liquid out into the vapor phase. We have seen that the surface energy γ_0 is the energy per unit area needed to form a surface.

The molecular volume, V, given in this table is the volume of the liquid divided by the number of molecules. The molecular surface, S, is the surface of a sphere which has the volume V.

The extremely low values of λ, the heat of evaporation, per molecule, for helium and hydrogen, indicate that the forces exerted by these molecules on their neighbors are unusually weak. This is in accord with the great stability of the electron pair which forms the K shell of atoms and the covalence bond. The diameters of the helium atom and hydrogen molecule given by the kinetic theory from viscosity measurements, viz., 1.9 and 2.4 A.U., correspond to volumes V of only 3.6 and 7.2 A.U.^{3}, which are very small compared to the volumes occupied in the liquid. This very open structure of the liquid is again an indication of the weak attractive forces between these molecules.

The effect of replacing one of the hydrogen atoms in the hydrogen molecule by the hydroxyl radical, thus producing water, is to decrease the value of V from 47. to 30., an indication of strong forces acting between the hydroxyl groups which compress the liquid. A better measure of these forces is given by the fortyfold increase in the value of λ from 1.67 to 67. The surface energy γ_0 has been increased twenty-fourfold.

The data for argon illustrate the properties of an atom having a complete electron shell or octet. The fact that in spite of the much larger electron configuration (with a kinetic theory diameter of 2.9) the volume per molecule in the liquid is the same as for hydrogen shows that the field of force around the molecule is far greater than for hydrogen and helium. The heat of evaporation per unit area, λ/S, is a very convenient measure of the intensity of this field. With hydrogen, helium, and argon it is about one-half of the surface energy γ_0.

The data for methane indicate that this molecule has a value of λ/S about the same as that for argon. This molecule has a completed octet which shares pairs of electrons with hydrogen atoms. Evidently the presence of the hydrogen atoms does not appreciably alter the field of force; the main effect is to raise the molecular volume, thus raising λ and the boiling point T_B almost in proportion to S.

The values for λ/S for the saturated aliphatic hydrocarbons beyond propane are practically constant and equal to 28. The same constancy is shown in the surface energy γ_0. The data for octane shown in table 1 are typical. The surfaces of the molecules of the higher saturated hydrocarbons are thus very much like those of argon atoms, the effect of the chain formation manifesting itself principally in the increase in λ/S from 18 to 28.

The constancy of λ/S is also an indication that the molecules of the higher hydrocarbons are approximately spherical in form. The known flexibility of the chain and the surface energy reduction resulting from the more compact form afford ample explanation of this spherical form.

The effect of substituting a hydrogen atom in octane by a hydroxyl radical is illustrated in the last line of the table by the data for *n*-octyl alcohol. There is a small decrease in V paralleling that observed in water, except that now, since each OH group in the liquid cannot be close to many other OH groups, the decrease in volume is considerably less. The large field of force around the OH group is best illustrated by the increase of 26 units in the value of λ. The fact that this increase is less than half of that observed in the change from H_2 to H_2O shows that the OH group in the molecule of the vapor of octyl alcohol is able to bury itself, at least in part, in the approximately spherical molecule.

In spite of the large increase in λ and λ/S in octyl alcohol, the surface energy γ_0 is the same as for octane. This can be explained by the *orientation of the molecules* in the surface layer of octyl alcohol. The great attractive forces exerted by the hydroxyl groups cause them to be drawn down in the interior of the liquid. Thermal agitation tends to counteract this tendency. According to the Boltzmann equation, the relative distribution of molecules between two regions of differing energy is measured by $\exp(W/kT)$, where W is the difference in the energy of the molecule in the two states. Now, judging from a comparison of the values of λ for octane and octyl alcohol, the energy necessary to bring an OH group from a hydrocarbon environment out into free space is at least 26×10^{-14} erg. The energy corresponding to kT at room temperature is about 4×10^{-14} erg. Since W is thus more than 6.5 times as great as this, we may conclude that nearly all of the molecules (all but about $\exp(-6.5) = 10^{-3}$)

in the surface of octane will be oriented in such a way that the hydroxyl groups do not reach the surface.

We now may understand why the surface energy of octyl alcohol is the same as that of octane. We have previously seen that γ_0 can be determined by the energy needed to separate a prism into two parts. We may conceive of this separation as taking place in two steps. The molecules on the opposite sides of an imaginary dividing plane may first be oriented so that the hydroxyl groups are turned away from this plane leaving only the hydrocarbon parts of the molecule in contact with the plane surface. The two bodies of liquids are then separated from each other along this plane which would require only the same energy as for pure octane. Because of the orientation of the molecules, γ_0 thus differs from that of octane only by the amount of energy needed to turn the molecules around in the interior of the liquid, which is probably negligible.

Referring again to table 1 we see that a comparison of λ/S with γ_0 affords a measure of the effect of orientation. In general, for molecules with uniform fields of force λ/S is from 0.5 to 0.55 of the value of γ_0.

When, however, a part of the molecular surface has a much weaker field of force than that of other parts, the surface of the liquid consists principally or wholly of the least active parts, so that γ_0 is lower than normal. Thus for octyl alcohol λ/S is 0.82 of γ_0 while for water it is 1.18, indicating that the water molecule is very unsymmetrical and is strongly oriented at the surface.

At present these illustrations will suffice. In a paper published in 1916 I showed that this theory was applicable to the surface tension of organic liquids in general, including cases of substituted benzene derivatives where the values of γ_0 depend to a marked degree on the relative positions of the substituted groups. Somewhat later W. D. Harkins and his coworkers investigated large numbers of organic substances in this way and completely demonstrated the importance of orientation of molecules in the surface layer of liquids consisting of unsymmetrical molecules.

OIL FILMS ON WATER (18, 21)

When a pure saturated liquid hydrocarbon is placed upon water, it remains on the surface as a drop or globule which has no effect on the surface tension of the surrounding water. If, however, an insoluble fatty or oily substance, such as the common vegetable and animal oils, is placed upon clean water, it spreads out almost instantly as a thin film over the surface. If the motions of the surface are made visible by dusting the surface with powdered talc, it may be seen that, with a limited amount of oil, the film only spreads out sufficiently to cover a definite area, or at least if the area exceeds a rather definite value, the oil has no effect on the surface tension of the water. A comparison of various insoluble organic substances has proved that the spreading tendency depends upon the presence of certain active groups or radicals in the organic molecule, these being the groups which tend to increase the solubility of organic substances in water. For example, pentane, C_5H_{12}, is practically insoluble in water but amyl alcohol, $C_5H_{11}OH$, is relatively soluble. Thus the hydroxyl groups in organic molecules exert strong attractive forces on the hydroxyl groups in the water molecules and these manifest themselves by an increase in solubility. Similarly the carboxyl group, COOH, tends to make the lower fatty acids much more soluble in water than the corresponding hydrocarbons.

Hydrocarbons with high molecular weight, such as $C_{18}H_{38}$, are extremely insoluble in water. If the carboxyl group replaces the CH_3 group at the end of the $C_{18}H_{38}$ chain, one end of the molecule only tends to dissolve in water, whereas the rest of the molecule still retains the insolubility of the hydrocarbons. By spreading over the surface of the water, molecules of this kind can bring their carboxyl groups in contact with the water without separating from one another.

An oil film formed in this way must consist of a single layer of molecules packed closely on the surface layer of the water. If there is a surplus of the fatty acid, as compared with the limited area over which it can spread, the endeavor of the carboxyl groups to come in contact with water causes the molecules to become so crowded at the surface that they stand nearly erect, side by side on the surface. The area occupied by each molecule is thus determined by the cross section of the hydrocarbon chain or by that of the head in contact with water, if this happens to be larger than the cross section of the chain. The thickness of the film is then determined by the length of the hydrocarbon chain.

By dissolving known weights of liquid or solid, oily or fatty substances in a volatile solvent such as hexane, and placing known amounts of these dilute solutions on the water surface, a definite number of molecules can be transferred to the water surface. The oil film can be confined to a given portion of the surface of water in a long tray by a floating strip of paper reaching across the tray. By measuring the forces exerted on the strip of paper, it is possible to measure directly the spreading force F in dynes per centimeter exerted by an oil film having a given number of molecules of oil per square centimeter of surface. This surface concentration we shall denote by the symbol σ. Such measurements as these, by which F can be expressed as a function of σ and T, give us then the two-dimensional equation of state of the oil film, which corresponds exactly to the three-dimensional equation of state which characterizes ordinary gases and liquids. In fact, the movable paper strip in these experiments is the equivalent of a piston which compresses the gas in a cylinder.

The oil films observed on water may exist as two-dimensional solids, liquids, or gases. The film on water obtained from stearic acid, $C_{17}H_{35}COOH$, is solid. If it is compressed by a force of 10 dynes per centimeter exerted against the paper strip, this solidity is manifested if particles of talc are dusted on to the surface and the effects of air currents directed against the surface are watched. The talc particles do not move freely over the surface; if a strong wind displaces them, they return to their original positions when the wind stops, proving a surface rigidity and elasticity characteristic of solids. Other substances such as cetyl alcohol or oleic acid give films which are liquid, since the talc particles circulate freely when small forces are exerted by the wind.

By slightly increasing the area available for these films of saturated fatty acids, it is found that the spreading force decreases very nearly to zero, which proves that these films do not act as two-dimensional gases but rather as two-dimensional liquids which have an unmeasurably small two-dimensional vapor pressure. With myristic acid (22), however, a definite two-dimensional vapor pressure of about 0.2 dyne cm.$^{-2}$ is observed. Still lower fatty acids give typical gaseous films, but they cannot be studied by this method because the films are so easily soluble in water that the force exerted by a moving barrier causes them to go into solution.

ADSORBED FILMS ON SOLUTIONS (18, 21)

The foregoing method for studying the properties of oil films on water is inapplicable if the film is soluble or is volatile. In such cases measurements must be made in the presence of saturated vapor or saturated solution. Gibbs' equation, equation 1, gives us a means of determining the relation between the amount adsorbed on the solution and the spreading force F, in terms of the partial pressure, p, of the vapor of the adsorbed substance over the liquid or the partial osmotic pressure, p, of the dissolved substance in the underlying solution. Experimentally F can be measured as the decrease in the surface tension of the pure liquid produced by the presence of the dissolved substance. By the integration of this equation, using the experimentally determined values of F, one can obtain the equation of state of the two-dimensional film whether this is gaseous or liquid or solid.

For very high or very low surface concentrations, Gibbs' equation takes simple limiting forms. At very low concentrations the molecules in the adsorbed films are so far apart that they exert no appreciable forces on one another. Under such conditions σ, the surface concentration, will be proportional to the volume concentration, which in turn is proportional to p. If we solve equation 1 on the assumption that σ is proportional to p, we find that it leads to the following equation of state

$$F = \sigma kT \tag{6}$$

which is the two-dimensional analogue of equation 3, the equation of state of an ideal gas, and it may therefore be called an equation of state of an ideal two-dimensional gas.

The effect of forces acting between the adsorbed molecules is to modify this equation. A two-dimensional analogue of the van der Waals equation can be written in the form

$$F = \frac{\sigma kT}{(1 - \sigma/\sigma_1)} + a\sigma^2 \tag{7}$$

where a and σ_1 are constants.

When the gas phase or the liquid phase contains a relatively high concentration, the concentration of the molecules in the adsorbed film tends to increase to a limiting value σ_1 corresponding to a complete monomolecular adsorbed film such as those that we observed in the study of oil films on water. Although such films show surface elasticity, that is, they are compressible, the forces required to compress the liquid and solid films are so much greater than those required to compress the gaseous film that the surface compressibility can be neglected as the first approximation, so that we can consider σ_1 to be approximately constant, that is, independent of p and F. Making this substitution in equation 1 and integrating, we obtain the following equation, which should be applicable for concentrated surface films

$$F = \sigma_1 kT \ln (p/p_0) \tag{8}$$

These two limiting equations are completely in accord with the general relationships found by J. Traube (23). In equation 8 p_0 is an integration constant whose value cannot be found from Gibbs' equation.

From the Boltzmann equation we can estimate the energy change, λ, involved in bringing a molecule from the vapor or liquid phase to the surface phase. We thus have

$$\sigma/p = \text{const. } \exp(\lambda/kT) \tag{9}$$

Traube found that with molecules of aliphatic compounds having different lengths of hydrocarbon chains, the ratio F/p for dilute solutions (which should be proportional to σ/p) increases about threefold for each CH_2. When this is interpreted in accord with Gibbs' and Boltzmann's equations, we conclude that the energy, λ, involved in the adsorption of these molecules increases linearly with the length of the chain. This means that each CH_2 group in the molecule must be similarly situated in the surface film. In other words, in these dilute films where there is much free water surface available, the hydrocarbon chains must lie flat on the surface. With the concentrated films in which σ is constant so that equation 8 applies, there is no available free surface of water and the molecules must stand nearly erect on the surface.

These two cases given by equations 6 and 8 are only limiting cases and the complete equation of state for the whole range from dilute to concentrated films would be more complicated, since it must involve the intermediate states between those in which the molecules lie flat on the surface and stand erect on the surface. The experimental difficulties of the accurate measurements of the surface tensions of solutions is such that relatively little work has been done on the equation of state of these adsorbed films on solutions as compared with the large amount of work done by N. K. Adam (22) and others on the equations of state of films of insoluble substances on water.

The molecules in adsorbed films on liquids are of course free to move over the surface of the liquid, except in so far as the film itself may possess the properties of a solid.

ADSORBED FILMS ON SOLIDS

Adsorbed films on solids may exist in three states corresponding to two-dimensional gases, liquids, or solids. A new factor now appears, however, which was not present in the case of adsorbed films on liquids. The forces exerted by the underlying solid on adsorbed atoms or molecules tend to hold the molecules in definite positions fixed by the lattice of the solid. The solid surface is thus to be looked upon as a type of checkerboard containing definite numbers and arrangements of elementary spaces (13, 24), each of which is capable of holding an adsorbed molecule. To move a molecule from one elementary space to another thus presumably requires something analogous to an activation energy; only those molecules possessing a sufficient kinetic energy to pass over a potential barrier can succeed in hopping from one elementary space to another (25). On this basis we should expect a surface mobility at high temperatures which would disappear at low temperatures. The logarithm of the rate of mobility, or the surface diffusion coefficient, should vary linearly with the reciprocal of the absolute temperature and the slope of this line should be proportional to the activation energy.

In general the surface diffusion coefficient increases with σ for the ability of adatoms to cross the potential barrier is not determined solely by the thermal agitation of the molecules but depends on $dF/d\sigma$, since differences in the value of F over the surface contribute to the mobility.

We may thus consider that in general the adatoms on solids move over the surface by hopping between elementary spaces. If the adatoms move nearly independently of one another, so that they migrate freely on to all unoccupied portions of the surface, the adsorbed films can be regarded as a two-dimensional gas in spite of the fact that the atoms tend to occupy definite positions. Such films constitute a two-dimensional crystalline gas, the crystalline character being imparted by the underlying lattice. If attractive forces exist between the adatoms which are sufficiently strong to cause them to form a definite two-dimensional condensed phase in equilibrium with a two-dimensional vapor phase, we clearly have to do also with a two-dimensional solid or liquid. If the mobility is high, this condensed film may have properties characteristic of liquids; with no mobility at lower temperatures, the conditions will be analogous to that of a two-dimensional glass. A two-dimensional solid analogous to ordinary three-dimensional solids would exist only if the forces exerted by the adatoms on each other can keep them from slipping past one another.

CONDENSATION-EVAPORATION THEORY OF ADSORPTION ON SOLIDS

When molecules of a gas in contact with a solid impinge individually on the solid, they may either condense or may rebound from the solid as though elastically reflected. Those molecules that condense may subsequently evaporate. There is much theoretical and experimental evidence that a true reflection of molecules in these conditions is a rather abnormal occurrence;

although the specular reflection of molecular rays from certain crystalline surfaces shows that it sometimes exists. In the great majority of cases, however, the observed phenomena indicate that the larger part of all incident molecules condense on the surface and reach thermal equilibrium with it before they evaporate (26, 27). With such gases as hydrogen and helium, accommodation coefficients materially less than unity have been found. In general these occur with gases striking solids at such temperatures that the rate of evaporation may be assumed to be so high that the life of the condensed molecule is of the order of 10^{-13} second, which is about the time required for a molecule to perform a single thermal oscillation on the surface. Under these conditions it is not surprising that thermal equilibrium is not reached.

When the rate at which molecules impinge on the surface is μ, as given by equation 4, and ν is the rate at which they evaporate (molecules cm.$^{-2}$ sec.$^{-1}$), then the rate at which they accumulate on the surface is given by

$$\frac{d\sigma}{dt} = \alpha\mu - \nu \tag{10}$$

where α, the condensation coefficient, in the majority of cases is equal to unity, but in any case can never exceed unity. The rate of evaporation ν is in general dependent on the temperature and on σ, the surface concentration. Of course it also depends on the nature of the solid surface on which adsorption occurs. If the surface is strictly homogeneous, ν may be a function of σ and T only for a given surface, but it may be possible that different portions of the surface are capable of exerting different forces on adatoms so that ν and σ may not be uniform over the surface.

In a stationary state when σ is not changing with time, the general condition that must be fulfilled is

$$\alpha\mu \tag{11}$$

If we divide the rate of evaporation, ν, by σ, the number of atoms per square centimeter, we obtain the average probability per second for the evaporation of the individual atoms. The reciprocal of this, τ, is thus the average life of an adatom on the surface. Thus we have

$$\tau = \sigma/\nu \tag{12}$$

This time lag that exists between the condensation and the evaporation of adatoms may thus be looked upon as the fundamental cause of the adsorption of gases on solid surfaces.

In general, ν should increase rapidly with temperature as the vapor pressure of a substance does. Thus the logarithm of ν should increase approximately linearly when plotted against the reciprocal of the absolute temperature, and the slope of this line is proportional to the heat of evaporation and is a measure of the magnitude of the forces by which the adatoms are held on the surface. Thus ν should be approximately given by an equation of the type

$$\nu = \text{const.} \exp(-\lambda/kT) \tag{13}$$

where λ is a measure of the energy required to remove an adatom from the surface. The large variations of ν for different substances are due mainly to variations of λ rather than to differences (28) in the constant factor in equation 13. This is indicated by such approximate rules as Trouton's law.

The forces acting between atoms and molecules are normally of extremely short range (27, 29) so that the forces acting on an adatom which determine the magnitude of λ and therefore ν, depend mainly upon the atoms with which any given adatom is in contact. When the gas pressure is raised or the temperature is lowered so that σ increases to such a point that there is no longer room for any additional molecules in the first layer in contact with the solid, a still further increase in σ would require that a large number of adatoms must be contained in a second layer. Now these adatoms in the second layer cannot be in *contact* with the solid surface on which the primary adsorption occurs and therefore for these atoms λ_2 should differ from the value of λ_1 that applies to the adatoms in the first layer. Since λ occurs in the exponent of equation 13, a relatively small change in λ is sufficient to cause a marked difference in the value of ν.

Thus when the adsorbed substance is not nearly identical in its properties with the substance on which adsorption occurs, we should expect the value of ν for atoms in the first and atoms in the second layer to be greatly different from one another. Naturally two cases may arise; ν_2 may be either greater or less than ν_1 (Reference 28, pp. 2811 and 2815).

Case I. $\nu_2 < \nu_1$

If ν_2 is less than ν_1 the atoms in the second layer are held by stronger forces to those in the first layer than these latter are by the atoms of the underlying solid. There is therefore a tendency for the atoms in the first layer to form clusters and on these clusters the second and third, etc., layers begin to form long before the whole of the first layer is covered (27). Such phenomena are of common occurrence. For example, when mercury, cadmium, or iodine are vaporized in vacuum and are condensed on a glass surface, at not too low a temperature, discrete crystals of the condensed substances form on the glass. This is a direct indication that these atoms exert greater forces on one another than they do to the underlying glass.

If the glass surface is maintained at a temperature so high that these nuclei do not form, then the glass surface *appears* to reflect all the incident atoms, for they evaporate from the glass surface far more rapidly than they do from a cadmium surface at the same temperature. Such observations were made by R. W. Wood, who attempted to explain them by a large reflection coefficient. He believed that experiments indicated that molecules of mercury incident at low pressures on cold glass surfaces were completely reflected at temperatures above −90°C., but were completely condensed below that temperature.

From our present viewpoint such a critical temperature has nothing to do with a true reflection but is dependent on the fact that with a given stream of mercury or cadmium atoms there is a definite temperature below which evaporation of the individual adatoms cannot take place fast enough to prevent accumulation sufficient to form a monatomic film so that all further evaporation at these low temperatures ceases. Experiments show conclusively that at all temperatures the mercury atoms condense but that, if the temperature conditions are favorable, single atoms re-evaporate from the glass at fairly low temperatures.

It is evident therefore that those cases in which ν_2 is less than ν_1 are characterized by the growth of crystals from nuclei and do not lead to the formation of monomolecular films but rather to discrete crystal particles.

Case 2. $\nu_2 > \nu_1$

In this case, as the pressure is gradually raised or the temperature is lowered, σ increases until a monomolecular film is formed, but it then takes a considerable decrease in temperature or increase in pressure before a second layer begins to form. These conditions therefore commonly lead to the formation of films which do not exceed a molecule in thickness over a wide range of experimental conditions. This case therefore is characterized by typical adsorbed films.

ADSORPTION ISOTHERMS

The fundamental equation governing the amount of adsorbed substances on a solid surface is given by equation 11. To put this into a definite form relating the pressure, p, of the external gas and σ, the surface concentration, we need only to be able to express α and ν as functions of σ and T. The functional relation of ν to σ depends not only on the forces exerted by the underlying solid, but on the forces acting between adatoms. Furthermore we must consider that the incident molecules corresponding to μ cannot all go directly into elementary spaces on the bare surface, but many of them will make their first contact at places already occupied by adatoms. An important aspect of the problem of the adsorption isotherm is the determination of the manner in which these incident atoms find places in the first layer. Many atoms may temporarily be forced to occupy places in the second layer from which they can either evaporate at a much higher rate than from the first layer, or may migrate until they drop into positions in the first layer.

It is natural under these conditions to make assumptions which are as simple as possible and to see whether the resulting equations can find a field of application (24). If the adatoms do not exert appreciable forces on one another, we may thus assume that the life, τ, of each one is independent of the presence of other atoms on the surface. Thus by equation 12 ν is proportional to σ.

Instead of dealing with the surface concentration σ it is often convenient to use the covering fraction Θ defined by

$$\Theta = \sigma/\sigma_1 \tag{14}$$

where σ_1 is the surface concentration in a complete monomolecular film.

Thus we may put

$$\nu = \nu_1\Theta \tag{15}$$

where ν_1 represents the rate of evaporation from a completely covered surface.

When molecules incident on the surface strike a part which is unoccupied by other adatoms, we may assume that the fraction α_0 condenses. The fraction of such surface which is bare may be represented by $1 - \Theta$. Therefore the number of incident atoms which go directly into the first layer may be put equal to $\alpha_0(1 - \Theta)\mu$. The fate of the other incident atoms, viz., those that first strike adsorbed atoms, will depend on many factors, some of which we shall discuss later. A very simple, although not very probable, assumption is that all these atoms reëvaporate so fast that they do not have opportunities to find positions in the first layer. On these assumptions we find

$$\alpha\mu = \alpha_0(1 - \Theta)\mu \tag{16}$$

Substituting this and equation 15 into equation 11 and solving for Θ, we obtain the following simple adsorption isotherm,

$$\Theta = \frac{\alpha_0\mu}{\nu_1 + \alpha_0\mu} \tag{17}$$

This equation has been found to apply with reasonable accuracy to a surprisingly large number of cases of adsorption on plane surfaces. Considering the nature of the simplifying assumptions made in its derivation, it should of course not be looked upon as a general equation for the adsorption isotherm. The cases where this equation is most likely to apply are those in which the adsorption occurs only in elementary spaces which are so far separated from one another that the adatoms in the separate spaces do not exert appreciable forces on one another. This can justify the assumption of equation 15. Also in this case the condensation may reasonably occur according to equation 16, because if a given space is occupied, which has a probability proportional to Θ, the incident atom cannot merely slip into an adjacent elementary space but must fall on to areas on which it is held with so little force that it evaporates before it can move into any vacant elementary space. These assumptions will give us an equation like equation 17 except that the significance of Θ and of the coefficient α_0 is somewhat modified.

Recent experiments have shown that in the mechanism of condensation mobility plays an important part (30). Thus in general an incident molecule striking a surface already covered may be assumed to move an appreciable distance before finally settling into a position in the first layer. Certainly if the surface is homogeneous so that all parts of it are available for adsorption, an incident molecule striking an isolated adsorbed molecule can hardly be regarded as being even temporarily in a second layer. Such an atom will slip into a position in the first layer before having any occasion to rebound or evaporate from the surface. An atom cannot be in a second layer even temporarily unless it is supported by at least three or more often four atoms in the underlying layer. Even if there is no mobility, the probability that an incident atom could occupy a place in the second layer would be proportional to Θ^n, where n is at least as great as 3 or 4. If the rate of evaporation is very high, we might expect these atoms to evaporate before finding places in the first layer. On this basis, therefore, instead of equation 16, the expression for the rate of arrival of atoms in the first layer should be

$$\alpha\mu = \alpha_0(1 - \Theta^n)\mu \tag{18}$$

Some experiments were made to test the reasonableness of these conclusions. The bottom of a tray was covered with steel balls

($\frac{3}{8}$ inch diameter) closely packed into a square lattice and cemented into position. This surface thus possessed many of the features of a homogeneous crystal surface, the steel balls corresponding to the individual atoms. When other balls of the same size were thrown on to the surface, they occupied definite elementary spaces, each being in contact with four underlying balls. The number of such elementary spaces (except for an edge correction) was the same as the number of balls which were cemented into place (zero$^{\text{th}}$ layer). A large number of balls, sufficient to cover the fraction θ of the available spaces, was placed in the tray (in first layer) and the tray was shaken to give a random distribution. A small number of additional balls were then dropped at random from a height of 5 cm. to the surface, and the number of these which went into the second layer was counted. It was found that the probability, P, that a given incident ball would occupy a position in the second layer was quite accurately given by

$$P = \theta^{4.5} \tag{19}$$

The fraction of the incident balls finding positions in the first layer was thus $1 - \theta^{4.5}$. Comparing this with equation 18 gives a value of $n = 4.5$. The reason that n is greater than 4, the number of underlying atoms, is probably that the kinetic energy of the balls causes some of them to roll from their positions of first contact.

Applying these results to adsorption we should expect that until θ is very close to unity, all atoms incident on the surface should reach positions in the first layer without any opportunity of evaporation or reflection even if the evaporation rate in the second layer is very high.

EFFECT OF FORCES ACTING BETWEEN ADATOMS (28)

The fact that two adatoms cannot occupy the same elementary space at the same time must mean that they exert repulsive forces on one another. This will manifest itself in the equation of state of the adsorbed atoms by a factor such as the $1 - \theta$ in the denominator of the first term of the second member of equation 7. This means that the spreading force tends to rise indefinitely as θ

approaches the value unity. Combining this equation of state with Gibbs' equation, and assuming $\alpha = 1$, we obtain for an adsorption isotherm the equation

$$\ln (\nu/\Theta) = \ln (1/(1 - \Theta)) + 1/(1 - \Theta) + \text{const.} \tag{20}$$

Thus we see that the rate of evaporation should increase indefinitely as Θ approaches unity. It is just this effect which limits the amount of material in typical adsorbed films on liquids or solids to that contained in a monomolecular layer.

The forces holding adatoms on the surface in characteristic cases of adsorption are usually far greater than those acting between adatoms. If this were not the case, we would be dealing normally with the case in which ν_2 is less than ν_1 so that we would not have adsorbed films but crystal nuclei. The effect of these strong forces originating from the underlying surface is to polarize the adatoms. If these are all of one kind, they thus tend to become similarly oriented dipoles which repel one another with a force varying inversely as the fourth power of the distance between them. There may also be attractive forces of the van der Waals type, but these will vary with a much higher power of the distance. The dipole forces will have a range of action far greater than other forces involved. A knowledge of these factors which are probably important in most cases of adsorption can best be undertaken by a detailed study of some one example in which quantitative determinations of all the factors are possible. The example that I have chosen for this purpose is that of adsorption of cesium vapor on tungsten, for in this case we can measure with great precision the surface concentration σ as well as the rates of evaporation, ν, of atoms, of ions, and of electrons (30). Thus we are able to express these values of ν_a, ν_p, and ν_e as functions of Θ and T. These measurements enable us not only to determine the forces acting between the adatoms, but to determine the electrical properties of the adsorbed films.

CESIUM FILMS ON TUNGSTEN

The ionizing potential of cesium is 3.9 volts, which is lower than that of any other chemical element. The heat of evaporation of electrons from tungsten corresponds to 4.6 volts. Thus the energy necessary to detach an electron from a cesium atom is 0.7 volt less than that necessary to pull an electron out of metallic tungsten. It is therefore not surprising that experiments (31, 32) show that every cesium atom which strikes a tungsten filament at high temperature loses its electron and escapes as a cesium ion. The electric current that thus flows from the tungsten is a quantitative measure of the number of atoms of cesium that strike the filament. Since currents 10^{-17} ampere can be measured by an electrometer, it thus becomes possible to detect a pressure of cesium vapor so low that only one hundred cesium atoms per second strike the surface of a filament.

The escape of the cesium ions from the tungsten surface is an evaporation phenomenon. If the temperature is below about 1100°K., the rate of evaporation of the ions may be so low that it does not keep pace with the rate at which the atoms arrive, so that there is an accumulation of adsorbed cesium on the surface. As a matter of fact, the rate of evaporation of the adsorbed cesium from the surface at one thousand degrees is about the same as that from a surface of metallic cesium at room temperature (300°K.). Thus from Trouton's rule we should expect the heat of evaporation of cesium adatoms to be about three times as great as the heat of evaporation of cesium itself.

Such large forces between the adsorbed cesium atoms and the underlying tungsten surface are to be expected as a result of the fact that the cesium tends to lose its electron when close to the tungsten surface. Thus the positively charged cesium ion induces into the conducting tungsten surface a negative charge which exerts a force of attraction on the ion (the "image force") equal to $e^2/4x^2$, where x is the distance of the ion from the surface. This image force is of ample magnitude to account for the strong forces holding cesium on tungsten.

If a thoriated tungsten filament is used, and this is given the special heat treatment required to bring a complete monatomic film of thorium to the surface, the heat of evaporation of electrons falls to about 3 volts, which is 0.9 of a volt lower than the ionizing potential of cesium. In accord with this fact the experiments show that cesium atoms are not converted into ions by an activated thoriated filament, nor is there any observable tendency for the cesium to become adsorbed on the filament.

If with a pure tungsten filament in presence of cesium vapor, the temperature is maintained low enough to permit an adsorbed film of cesium to be formed, the positively charged adatoms, which cause a positive contact potential against the pure tungsten surface, have the effect of lowering the heat of evaporation of the electrons. When such an amount of cesium is present on the surface that the heat of evaporation is materially below 3.9 volts, the tendency of the filament to rob incoming cesium atoms of their electrons and thus allow them to escape as ions, is lost. This means that ν_p, the rate of evaporation of ions, becomes very small as Θ, the fraction of the surface covered by cesium atoms, increases.

At temperatures of about 700°K., in presence of cesium vapor saturated at room temperature (pressure about 10^{-9} atmospheres), Θ increases to approximately 0.7 and the heat of evaporation has then been lowered to such a point that the electron emission is 10^{22} times greater than that of a clean tungsten filament at the same temperature.

Within the last three years, Dr. J. B. Taylor and I have made a detailed study (28, 30) of the rates of evaporation of atoms, ions, and electrons from these cesium films on tungsten as functions of Θ and T. In order to measure Θ, a method was devised for determining σ, the number of adsorbed atoms per square centimeter of tungsten surface. Two methods were found. When Θ is less than 0.08, a sudden heating or flashing of the filament at temperatures above 1300°K. causes every cesium adatom to escape from the filament as an ion so that the ballistic kick measured with the galvanometer gives directly the value of σ. The second method, which is applicable at any values of σ (even those corresponding to polyatomic layers), involves the evaporation of the adatoms as atoms, in the presence of a retarding field which prevents the escape of ions. This burst of atoms falls on a parallel neighboring tungsten filament heated above 1300°K. from which these atoms escape as ions. The ballistic kick of current from this second filament thus measures σ on the first filament. We call this the two-filament method of measuring σ.

The measurements of σ showed that as the cesium pressure is increased or the filament temperature lowered, σ increases to a definite limiting value of σ_1 which is 4.8×10^{14} atoms per square centimeter of apparent filament surface. A study of the crystal habits of tungsten has shown that the surface lattice of surfaces etched by evaporation contains 1.425×10^{15} atoms per square centimeter. Since the diameter of the cesium atoms is almost exactly twice that of tungsten, and because of the tendency of the adatoms under the strong forces exerted by the tungsten, to occupy definite elementary spaces on the surface, we conclude that the maximum number of cesium adatoms is one-quarter the number of tungsten atoms and therefore the true value of σ_1 is 3.563×10^{14} atoms per square centimeter. Comparing this with the observed or apparent value of σ_1 it appears that the true surface of the tungsten filament is 1.347 times the apparent surface, this difference being due to the slight etching of the filament surface by evaporation at high temperatures.

A study of transient states during which θ increases or decreases with time have proved conclusively that the phenomena of condensation or evaporation go on independently of one another, the condensation being dependent on μ, while the evaporation ν is strictly a function of θ and T only and does not depend upon the way the surface film has been formed.

The experiments show that within the accuracy of the experiments (about 0.5 per cent) the condensation coefficient α is always equal to unity even when θ is as great as 0.98. This proves that the incident atoms, which under these conditions must nearly all strike adatoms, can slide around in a second layer until they find positions in the first layer. The experiments prove, however, that the number of atoms which exist at any time in the second layer is extremely minute, of the order of 10^{-7}. The atoms in the second layer possess very high surface mobility.

The rate of evaporation of atoms ν_a increases at any given temperature extremely rapidly as θ increases. Thus at 1000°K. an increase of θ from 0.1 to 0.9 causes a 10^{11}-fold increase in ν_a. This indicates very strong repulsive forces between the adatoms, in agreement with the fact that these adatoms tend to be positively charged as indicated by the effect of the film in increasing the electron emission. It has been possible to develop this relationship between ν_a and ν_e into a quantitative theory.

A single cesium adatom on a tungsten surface may be regarded as an ion held to the metal by its image force. The image and the ion thus constitute a dipole, having an electric moment, M, oriented with its axis perpendicular to the surface. Because of the strong electric fields close to the ion when it is adsorbed on the surface, we should expect the conduction electrons in the metal to be drawn towards the ion so that the dipole moment should be considerably less than we would calculate for a cesium ion at a distance from an ideal metal surface equal to its radius. The experimental values of M have actually been found to be 16.2×10^{-18}, whereas we calculate 25×10^{-18} for a spherical cesium ion in contact with an ideal conducting plane.

The force, f, between two such adion dipoles is given by

$$f = (3/2)\,M^2/r^4 \tag{21}$$

where r is the distance between the adions.

We may now work out the equation of state of the adsorbed cesium films in terms of these forces by means of Clausius' virial equation which for surfaces takes the form

$$F = \sigma kT + (1/4)\sigma\Sigma(rf) \tag{22}$$

where the summation is to extend over all adatoms which act on any one adatom. The forces, f, are of two kinds: first, the long range forces which correspond to the dipole repulsion given by equation 21, and second, the short range forces acting between atoms in contact which prevent any two from occupying a single elementary space at the same time. These short range forces may be taken into account by dividing the second member of equation 6 by $(1 - \Theta)$ as has already been done in equation 7. In this way by an integration process it has been possible to derive the general equation of state for adsorbed atoms which repel as dipoles. This equation is

$$F = \sigma kT/(1 - \Theta) + 3.34\,\sigma^{5/2}M^2 + 1.53 \times 10^{-5}\sigma^2 T^{1/3} M^{4/3} I \tag{23}$$

where I is an integral whose numerical value can never exceed 0.89 and which can be obtained from tables and curves from the value of M, σ, and σ_1.

The spreading force F calculated in this way cannot be measured directly for a solid surface but it can be related to the rate of evaporation, ν_a, by means of Gibbs' equation

$$\frac{dF}{d \ln \nu} = \sigma kT \tag{24}$$

By substituting in this equation the values of F from equation 23, ν_a can be calculated in terms of M. Actually we have reversed the process. From the experimentally determined values of ν_a as functions of σ and T, we have calculated F by equation 24 and from these by equation 23 have obtained M. These values of M are found to be functions of σ but are not appreciably dependent on T, although a slight dependence is indicated by the form of equation 23.

A test of this theory can be made since the values of M obtained from ν_a may be compared with values of M obtained from the contact potential which may in turn be obtained from measurements of ν_e. The contact potential, V, of a surface covered with an adsorbed film as compared with that of a pure metal surface is given by

$$V = 2\pi\sigma M \tag{25}$$

Furthermore the electron emission ν_e is related to the contact potential, V, by the Boltzmann equation

$$\nu_e/\nu_w = \exp(Ve/kT) \tag{26}$$

where ν_w is the electron emission from pure tungsten at the same temperature. The full line curve in figure 2 gives values of V calculated by equation 25 from M as determined from ν_a. The points shown by small circles represent values of V obtained from ν_e by equation 26.

The values of V obtained by these two independent methods agree nearly perfectly when $\Theta < 0.5$. The deviations at higher values of Θ seem to indicate that for high values of Θ the short range forces are somewhat greater than those given by the factor $1 - \Theta$, the denominator of the first term of the second member of equation 23. Calculation shows that for a value of $\Theta = 0.75$, that part of the spreading force which is due to the short range forces is actually 45 per cent greater than is given by the first term in the second member of equation 23.

It is also possible to calculate the contact potential from data on ν_p the rate of evaporation of ions from the surface. The values of ν_a, ν_e, and ν_p must be so related to one another that they

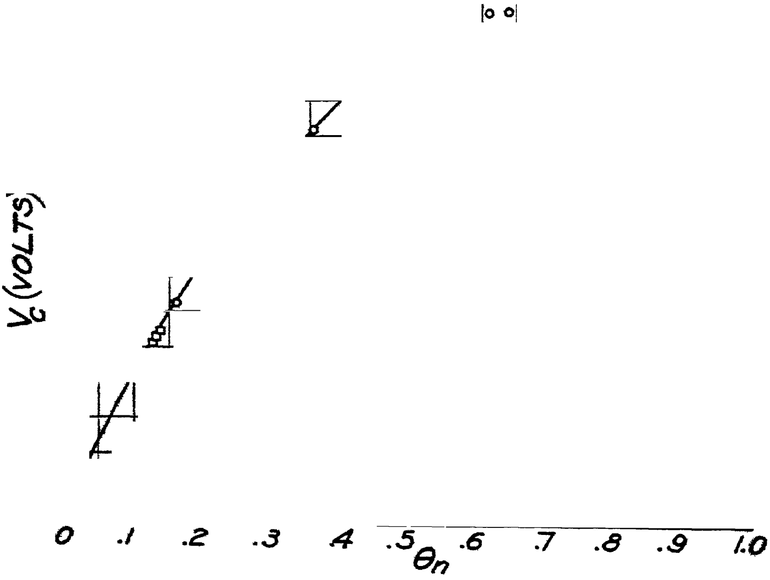

FIG. 2. CONTACT POTENTIAL OF CESIUM FILMS ON TUNGSTEN AGAINST CLEAN TUNGSTEN

give concentrations of atoms, electrons, and ions in the vapor space near the filament which agree with the thermodynamical requirement for equilibrium among these particles. We may thus put

$$n_e n_p / n_a = K \tag{27}$$

where K is the equilibrium constant that can be determined from the ionizing potential in accordance with the Saha equation.

When this is done, and we combine with the Boltzmann equation and the Dushman equation for the electron emission from tungsten, we obtain

$$\ln (2\nu_p) = \ln \nu_a + (e/kT)(V_w - V_i - V) \tag{28}$$

where V_i is the ionizing potential of cesium, and V_w is the heat of evaporation of electrons from tungsten. The values of the contact potential, V, calculated from ν_p in this way are indicated in figure 2 by squares. These points lie on the curve obtained from ν_a.

This agreement of the values of V obtained by these three methods shows that our theory gives a complete account of the electrical and chemical properties of moderately dilute adsorbed films of cesium on tungsten. It proves also that the surface of these tungsten filaments was essentially homogeneous, so that the probability of evaporation of any adatom or adion was independent of the position of the atoms on the surface and was determined wholly from the value of σ at that point.

The experiments showed, however, that this conclusion, although true for over 99 per cent of the surface, did not hold exactly. Deviations at very low values of Θ indicated that about 0.5 per cent of the surface consisted of what we may call active spots which adsorbed cesium far more strongly than the rest of the surface, so that the heat of evaporation of these areas was about 37 per cent greater than that for atoms on the normal part of the surface. Experiments also showed that adsorption on this part of the surface was of the type indicated by equation 17—the simple type of adsorption isotherm. This means that the atoms adsorbed in the active areas did not exert appreciable forces on one another. Evidently the active spots consist of separated elementary spaces distributed over the surface, probably near grain boundaries or at steps in the crystal faces.

A variation of the dipole moment M with σ results from the depolarizing effect of neighboring dipoles. The electric fields due to these dipoles can be calculated by an integration process similar to that used in calculation of F, and are of the order of 5×10^7 volts cm^{-1}.

When a tungsten filament is heated to about 1100°K. in cesium vapor and there is an accelerating field drawing ions from its surface, two coëxistent surface phases may occur. For one of these θ is about 0.15, while in the other it is very close to zero. The atoms that strike the less concentrated phase evaporate as ions, while those that strike the concentrated phase evaporate as atoms. The phase boundary is perfectly stable and stationary at a definite temperature in the presence of a given pressure of cesium. If the temperature is raised slightly, the phase boundary moves towards the concentrated phase, so that the whole filament gradually becomes bare; a lowering of the temperature causes the whole surface to become covered with the concentrated phase. A detailed analysis of the mechanism at the boundary between the phases which involves diffusion from one phase to the other, makes it possible to measure the surface diffusion coefficient D. Results have shown that

$$\log D = -0.70 - 3060/T$$

From the temperature coefficient of D it can be calculated that the surface diffusion activation energy is about 0.6 volt. This means that between each of the elementary spaces there is a potential barrier of the height of 0.6 volt over which the adatoms must hop in order to migrate over the surface.

The experimental methods involved in these studies of cesium films on tungsten are capable of very great accuracy and sensitiveness, so that they seem to offer a rich field for the detailed study of adsorption phenomena. Dr. Taylor and I are continuing work in this field. We are planning to make accurate comparisons between the properties of films of adsorbed cesium, rubidium, and potassium. We have developed a method of introducing definite small amounts of oxygen by diffusion through a heated silver tube. In this way known numbers of oxygen atoms may be placed on the surface of a tungsten filament, thus forming negative dipoles. These attract the positive cesium dipoles which tend to form clusters around them forming a kind of two-dimensional colloidal distribution of cesium. We hope by the detailed study of such systems to learn the effects not only of repulsive but also of attractive forces between adatoms. Experiments are also in progress to study the adsorption of cesium on tungsten surfaces containing known numbers of adsorbed thorium atoms.

In such ways as these, together with the methods involving the spreading of oil films on water, it becomes possible to determine the equations of states of two-dimensional gases, with nearly the the same degree of accuracy as in the three-dimensional case, but with the further advantage that the conditions are especially favorable for the determination of the mechanism of all of the processes involved.

TYPES OF ADSORPTION

The classical kinetic theory of gases, as for example in the treatment of viscosity by Sutherland and of the continuity of the transition from gas to liquid by van der Waals, led to the recognition of attractive forces between molecules at large distances and strong repulsive forces at short distances. The chemist has long known that exceptionally large attractive and repulsive forces are associated with the chemical union between adjacent atoms which he represents by the valence bond (primary valence) and weaker forces which he has called secondary valence forces usually correspond to other types of chemical combinations. The physicist has studied the forces between charged particles, such as ions and dipoles, and more recently has discovered the interchange forces which are best explained in terms of quantum mechanics.

In the structure of matter, there can be no fundamental distinction between chemical and physical forces; it has been customary to call a force *chemical* when it is more familiar to chemists and to call the same force *physical* when the physicist discovers an explanation of it. There are also usually no sharp dividing lines between attractive and repulsive forces or between the various kinds of attractive or repulsive forces. Nevertheless a recognition of various types of forces responsible for the stability of matter proves useful in classifying natural phenomena. Thus in a qualitative way we may consider the following types of forces (29).

(1) Coulomb forces between ions or ions and electrons varying with $1/r^2$ where r is the distance between ions. The best examples of these forces are in salt-like substances.

(2) Forces between dipoles which vary with $1/r^4$ and depend on the orientation of the dipole.

(3) Valence forces, associated with the sharing of electrons between atoms.

(4) van der Waals attractive forces, which depend on the mutual polarizability of molecules. These forces are usually considered to vary with $1/r^7$.

(5) Repulsive forces due to the mutual impenetrability of completed electronic shells. It is primarily these which determine the collision areas of molecules in the kinetic theory. Born and Mayer (33) find that the potential energy of these repulsive forces between two completed shells is given by

$$A \exp[(r_1 + r_2 - r)/r_0]$$

where r_1 and r_2 are the effective radii of the two shells and r_0 is a universal constant equal to 0.435 A.U., while A is another universal constant. This means that this type of repulsive force between two atoms can be expressed as a function of the distances between the *surfaces of the atoms*, this function being the same for nearly all atoms (or molecules) which have completed shells, regardless of their electric charge. From a consideration of several other properties of solids and liquids, I had previously drawn a similar conclusion (reference 20, pp. 529–531) that the repulsive forces should be regarded "as surface forces which should be expressed as functions of the distances between the surfaces of the atoms (fixed by the electron orbits) rather than in terms of the distances between the centers of the atoms." A consideration of van der Waals forces showed that for these also the "intensities of the fields around different non-polar molecules are practically identical when regarded as surface forces."

The fact that these repulsive forces, according to Born and Mayer, decrease to $1/e^{\text{th}}$ value for each increment of 0.435 A.U. in the distance between the atoms, indicates that they have a very small range of action.

(6) Electron pressures. The force that counterbalances the Coulomb attraction of the electrons and ions in the alkali metals, and probably in other metals, is that due to the pressure of the Fermi electron gas.

Since all of these forces can be effective at the surface as well as in the interiors of solids and liquids, they must take part in adsorption phenomena. There should thus be various types of adsorption corresponding to the several types of forces which hold the atoms or molecules on the surface. Let us consider some examples.

Cesium on tungsten

The cesium ions are held by Coulomb attractive forces (here a modified image force) to the underlying metal. The corresponding repulsive forces which hold the ion a definite distance from the surface (and thus determine the dipole moment *M*) result from the pressure gradient in the Fermi electron gas which extends beyond the lattice of tungsten atoms. The forces between the cesium adatoms are typical dipole repulsions.

Oxygen on tungsten or carbon

The attractive forces are probably typical valence forces. That they are not ordinary Coulomb forces, such as those effective in cesium adsorption, is suggested by a consideration of the relation of the contact potential to the heat of evaporation of the adatoms. A film of cesium which has the maximum effect on the electron emission ($\Theta = 0.67$) has a contact potential of +3.0 volts against tungsten, while the heat of evaporation of the adatoms corresponds to 1.9 electron volts. With an oxygen film produced when a tungsten filament at 1600°K. is in contact with oxygen at low pressure, the contact potential against tungsten at 1600°K. is −1.6 volts, but the heat of evaporation is about 7 volts.

The adsorption of oxygen, hydrogen and carbon monoxide on platinum (36) affords other examples of adsorption dependent on primary valence forces.

Oil films on water

In these cases the attractive forces that cause the active heads to spread over the surface are principally dipole forces between the heads and the water molecules with some contribution from van der Waals forces. Above the heads there is a hydrocarbon phase in which van der Waals forces and the repulsive forces between completed shells predominate.

Non-polar gases on glass

The adsorption of such gases as nitrogen, argon, etc., on glass or mica at low temperatures is determined by typical van der Waals forces (24).

ACTIVATED ADSORPTION

Because of the various types of adsorption that exist, a single gas may be adsorbed by a given surface in several different ways. At sufficiently low temperatures van der Waals forces alone would be sufficient to cause adsorption (van der Waals adsorption). At higher temperatures molecules on the surface may undergo chemical change and thus be held by valence forces. The heat of adsorption is then far greater than corresponds to the van der Waals adsorption. The only reason that such adsorption does not occur at low temperatures is that the reaction velocity of the chemical change may be too low. Since there is an activation energy associated with each such reaction, H. S. Taylor (34) has proposed the term *activated adsorption* for the adsorption which involves such chemical changes.

In some cases, such as the adsorption of cesium atoms on tungsten, the adsorption involves only the transfer of one electron and can thus occur at very low temperatures so that activation is not required, and only one type of adsorption is observed.

The distinction between van der Waals adsorption and activated adsorption (reference 24, pp. 1399–1400) was pointed out by the writer in 1918 and illustrated by the adsorption of carbon monoxide and of oxygen on platinum. At the temperature of liquid air and with a clean platinum surface in contact with carbon monoxide at a pressure of 16 baryes, the surface concentration σ of the adsorbed carbon monoxide was 3.9×10^{14} molecules cm.$^{-2}$, but, as the temperature of the platinum gradually rose to 20°C., σ *decreased* to 1.4×10^{14} and then *increased* again to 3.9×10^{14} and remained nearly constant until 200°C. had been reached. When oxygen was brought into contact with platinum at liquid air temperature, 1.5×10^{14} molecules cm.$^{-2}$ were adsorbed immediately. On raising the temperature to 20°C., σ increased very slowly (in 18 hours) to 3.0×10^{14}. At 360°C. σ rose to 4.8×10^{14}. It was concluded "that at liquid air temperature platinum adsorbs carbon monoxide in much the same way that glass does, that is, by secondary valence forces. With a moderate rise in temperature this gas is released, but in the neighborhood of room temperature the reaction velocity becomes sufficient for the platinum to react (primary valence) with the carbon monoxide to form a much more stable adsorbed film."

In a discussion of the mechanism of the dissociation of hydrogen on tungsten filaments in 1916 the writer (7) considered the possibility that the adsorbed hydrogen exists on the surface in two forms and that the velocity of interaction between these forms may determine the rate of production of atomic hydrogen. The mathematical formulation which was given is applicable to many cases of activated adsorption.

Within recent years H. S. Taylor (34) and his coworkers have discovered many cases of activated adsorption and have demonstrated their importance in an understanding of contact catalysis. The velocity of the activation reaction, which is often low even at a temperature of several hundred degrees, has been measured and the activation energy calculated. Other investigators have sought to explain these slow surface reactions by assuming solution of the adsorbed gas in the underlying substance, or slow penetration into cracks or capillary spaces.

That this cannot be a general explanation is proved by some experiments (35) that Dr. Blodgett and I have made on the thermal accommodation coefficient of hydrogen in contact with tungsten. At temperatures from 200°K. to 600°K. a stable adsorbed film of hydrogen on tungsten is formed which gives an accommodation coefficient α of about 0.22. As the temperature is raised, this film goes over slowly into a much more stable film which is characterized by a value of $\alpha = 0.14$. The reaction velocity is such that the formation of the stable film requires several minutes at 600°K. and a small fraction of a second at 900°K., indicating an activation energy of the order of at least 20 kg.-cal. per molecule. Since the accomodation coefficient is a purely surface property, these experiments prove that these two forms of hydrogen film are both monatomic films which probably represent two kinds of chemical binding by valence forces. At temperatures below liquid air temperature a clean tungsten surface would undoubtedly show also van der Waals adsorption of hydrogen. This would thus be a third kind of adsorbed film of hydrogen on tungsten.

CATALYTIC ACTION OF SURFACES

A monatomic film of oxygen on tungsten at 1500°K. acts as a catalytic poison for nearly all the reactions which would otherwise occur in contact with the tungsten surface (15). Thus the dissociation of hydrogen into atoms at 1500°K. is stopped by a trace of oxygen, as is also the decomposition of ammonia, methane, or cyanogen. The effect of the oxygen is to cover the surface so that the other gas cannot make contact with the tungsten surface.

Similarly hydrogen and carbon monoxide act as catalytic poisons on platinum surfaces (36). The rate at which carbon monoxide and oxygen combine in contact with platinum is proportional to the pressure of oxygen and inversely proportional to the pressure of the monoxide. The reaction velocity depends on that fraction of the platinum surface which is *not covered* by adsorbed molecules of carbon monoxide. The oxygen molecules that can become adsorbed in these vacant spots and so be adsorbed on the platinum surface can thus react with adjacent adsorbed molecules of carbon monoxide.

In numerous cases investigated, the action of a surface in catalyzing a gas reaction involves just such interaction between molecules adsorbed in adjacent elementary spaces on the surface. On this basis it is possible to develop (7, 13, 36) a "law of mass action" for the velocity of surface reactions by which the observed reaction velocities can be explained quantitatively. It has been pointed out (15) that reactions of this sort are extremely sensitive to the actual distances between the atoms in the surface of the catalyst. Thus with many surfaces there is only a relatively small fraction of the surface on which the reaction can occur with extreme rapidity, while over the larger part of the surface it takes place at a negligible rate. A quantum theory explanation of the importance of the spacing of the atoms in the catalyst has recently been given by Sherman and Eyring (37).

The presence of a second layer of adsorbed atoms or molecules, although this second layer may cover only a minute fraction of the surface, is often of great importance in the mechanism of gas reactions brought about by a surface catalyst.

Thus in the oxidation of heated tungsten filaments in oxygen at low pressures by which WO_3 is formed, the oxygen molecules incident on a surface already nearly completely covered by a monatomic film of oxygen atoms, condense and momentarily exist in a second adsorbed layer (reference 29, p. 473). Although the rate of evaporation from this second layer is so high that the surface concentration is very low, the adsorbed atoms or molecules in this layer move freely over the surface and thus fill up the holes in the first layer, formed when WO_3 molecules evaporate, far faster than would otherwise be possible. These atoms in the second layer can also interact with those in the first layer and with the underlying tungsten to form the molecules of WO_3 which escape from the surface.

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PYRIMIDINES: THEIR AMINO AND AMINOÖXY DERIVATIVES

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INTRODUCTION

The chemistry of the pyrimidines has never been completely systematized, and since a knowledge of this class of cyclic substances has become increasingly important as a result of recent developments in biochemistry, an attempt to organize this material is now being made. The field to be covered is so very extensive, however, that only one particular section of it can be reviewed at this time. A group, which includes the pyrimidine hydrocarbon cycle,[1] together with the amino and aminoöxy derivatives, has been selected because of the fact that it includes pivotal substances such as cytosine, 5-methylcytosine, and divicine, which have been shown to occur in different combinations in both plant and animal tissues. In order to show the position which these and certain other derivatives of pyrimidine occupy with respect to some of the fundamental problems of biochemistry, it seems desirable by way of an introduction to review briefly the relationships which have now been established between pyrimidines and their precursors in biochemistry,—the nucleic acids. This material is so very voluminous that it can be treated merely in outline and only so far as it serves as a necessary prelude to any systematic study of pyrimidine chemistry.

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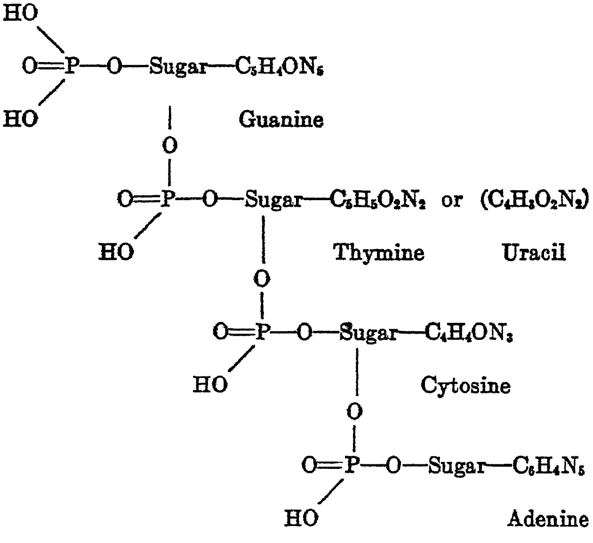
[1] Benzene being $(CH)_6$, pyrimidine is $(CH)_4N_2$.

The fact that the fundamental units of growth and reproduction are localized in the nucleus of the cell has long been recognized by biologists. It has also become of constantly increasing interest to chemists with the general acceptance of the idea that the characteristic features which serve to differentiate the cells of the different organs and also the cells of bacteria inimical to man, are to be found in the typical hydrolytic products which result from cell degradation. Of these the class of substances now generally known as "nucleic acids" is perhaps the most important. Developments in the investigation of substances belonging to this class have been exceedingly rapid in recent years, so that a number of fairly clearly defined individuals have been isolated and identified. Typical examples of substances of this kind are yeast nucleic acid, thymus nucleic acid, tuberculinic acid, etc. While it frequently happens that the name of the acid immediately suggests its origin, this is of course not always as obvious as in the case of the illustrations just mentioned.

A study of nucleic acids has led to the discovery that while they are extremely complex substances, a certain regularity is to be observed in the processes by means of which they suffer degradation into simpler units. The generally accepted structure of the nucleic acid molecule has been developed as a result of intensive research in many widely separated fields, but nevertheless embodies certain fairly simple fundamental conceptions. For example, all individuals belonging to this class may be assumed to result from the association of somewhat simpler aggregates known as *nucleotides*. This term is applied to substances which are formed by the association of phosphoric acid with certain still less complex organic aggregates known as *nucleosides*. The latter are glucosidic in character and are composed of sugars linked to nitrogenous substances spoken of as nuclein bases. Since the physical and chemical properties of any given nucleoside depend upon the nature of the particular sugar and nuclein base which enter into its composition, it has been found convenient to classify them as "purine-riboses," "pyrimidine-hexoses," etc., according to the character of their components.

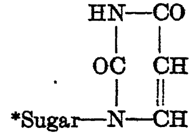
Such a classification accounts for the structure of the nucleoside only in the most superficial way, since any given sugar or base (purine or pyrimidine) is known to be capable of existing in a great variety of different modifications. Moreover, since the union between any given sugar and purine or pyrimidine is severed under the action of hydrolytic agents, and since both the sugar and the cyclic base thus separated are subject to a number of different structural transformations under the experimental conditions, it follows that the particular individuals which are isolated as a result of the resolution of such glucosidic combinations may not always correctly represent the particular sugar and base actually in union in the nucleoside. Furthermore, the exact nature of this union is still far from clear. For example, if the nucleoside is found to consist of a definite sugar linked to a pyrimidine the question as to the exact point of union in the case of each molecule has still to be answered. And up to the present time none of the answers to this particular question is sufficiently supported by experimental evidence to be completely satisfactory.

In order to present these general relationships in a somewhat more concrete form it is necessary to consider two typical nucleic acids in somewhat greater detail. Thymus nucleic and yeast nucleic acids have been the most thoroughly investigated, and most of the fundamental knowledge of nucleic acid structure has been acquired by the study of their degradation products. The discovery of this group of organic substances was first made by Miescher (152) in 1871, and the term "nucleic acid" was furnished by Altmann (1). The general method of preparation applied with modification by later workers was also furnished by this later investigator. The first fundamental contributions regarding the structure of nucleic acids were made by Kossel and his school of workers. These developments practically began with the year 1879 when Kossel began his work on nucleins in the laboratory of Hoppe-Seyler. His first publication dealt with the nucleic acid of yeast (120). The first important work on the chemistry of thymus nucleic acid was reported by Kossel and Neumann in 1894 (122), and through the investigations of Kossel, Steudel, and other workers in Europe since that date the partial elucidation of the structure of the highly complex nucleic acid molecule has been accomplished. It remained, however, for Levene and his many collaborators in this country to show that nucleic acids (thymus and yeast) are actually composed of nucleosides united with one another as complex esters of phosphoric acid. On hydrolysis the molecule is finally broken down into phosphoric acid and four different nucleosides representing combinations of a sugar with cytosine, thymine (or uracil), adenine, and guanine, respectively. Although neither the exact configuration of the sugar nor its point of linkage with any of these nitrogenous cycles has as yet been determined, the following diagram showing the general arrangement of these components is today commonly accepted by biochemists as representing roughly the configuration of a nucleic acid molecule.

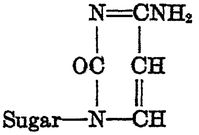


The outstanding difference in the constitutions of thymus and yeast nucleic acids revealed by recent research is to be found in the structure of the sugar group functioning in these two complex substances. The sugar component of thymus nucleic acid was concluded by Kossel and Neumann to be hexose, in view of its ready conversion on hydrolysis into levulinic acid. All workers on thymus nucleic acid held for years to this conception of the hexose nature of the sugar, until Feulgen (36) called attention to errors in the analytical figures of earlier work, and questioned the conclusions of the hexose structure of the sugar. It remained for Levene and London (139) to give support to Feulgen's conclusions. They took up again the study of nitrogen-free degradation products of thymus nucleic acid and actually succeeded in isolating the sugar complex and in proving it to be a desoxypentose. The irregularity of the behavior of thymus nucleic acid, as compared to that of yeast nucleic acid, was thus shown to be due to the peculiar chemical behavior of this sugar.

It has further been demonstrated conclusively by Levene and his coworkers that yeast nucleic acid may be resolved into four nucleosides which represent combinations of the pentose sugar *d*-ribose with cytosine, uracil, adenine, and guanine, respectively, and that these combinations are present in equimolecular quantities in the yeast nucleic acid molecule. It was observed, for example, that in the hydrolysis of this acid only a part of its phosphoric acid was split off, leaving a mixture of two phosphorated substances which were named *uridylic* and *cytidylic acids* (127, 136b, 137). These represent the first degradation units of the nucleic acid molecule and are called nucleotides. They break down on further hydrolysis into the nucleosides and phosphoric acid. In the case of the two examples cited the configuration of the two nucleosides may be represented respectively in the following way:



Uridine



Cytidine

*Sugar = *d*-ribose

For a complete account of the history and chemistry of nucleic acids the reader is referred to Monograph No. 56, entitled "Nucleic Acids", recently published under the auspices of the

American Chemical Society (135). The experimental evidence upon which the allocation of the sugar to the *N*-3-position in the pyrimidine ring depends will be reviewed later in connection with a somewhat detailed consideration of the various tests which may be applied in the detection of cytosine and its derivatives (136a, 138, 66d).

In this connection it may be noted that certain fundamental differences appear to exist in the sugar content of nucleic acids of animal or plant origin, the former yielding desoxypentose (*d*-ribodesose) (139, 142, 141) and the latter *pentose* sugars on hydrolysis. Fundamental differences have also been observed in the pyrimidine content of nucleic acids obtained from these two sources, since 5-methylcytosine and its deaminized product, thymine, are found among the degradation products of animal cells, while cytosine and its deaminized product, uracil, (but no thymine) are obtained along with other substances on intensive hydrolysis of plant tissues. Recently evidence has been obtained indicating that there may be exceptions to these observations leading to new generalizations of great significance.[2]

If, as has now been demonstrated, nucleic acids consist in part of pyrimidines in different forms of combination, any attempts to synthesize these extremely complicated aggregates must be based upon an exact and complete knowledge of the chemistry of the pyrimidines. This subject is, of course, too extensive for exhaustive treatment, but by confining the discussion in this paper to a limited section of this field, namely, to the reduced pyrimidines and their amino and aminoöxy derivatives, it will be possible to review the various types of syntheses and transformations which are typical of pyrimidines as a group, while avoiding many of the complicated problems which a complete survey of pyrimidine chemistry would involve.

Various individuals belonging to the general class of pyrimidines had been known for fifty years before Pinner in 1885 (161, 162a) called attention to the fact that all such substances could be regarded as derivatives of a ring structure closely analogous to pyridine:

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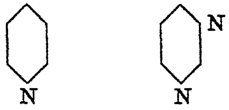
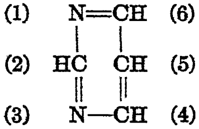
[2] Unpublished results.



Pyridine Pyrimidine

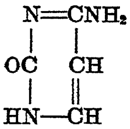
In other words, pyrimidine consists of a heterocyclic carbon–nitrogen ring, and as such possesses strongly basic properties. Like pyridine it reacts with mineral acids to form stable salts, and its hydrochloride combines with the chlorides of gold and platinum to form relatively insoluble complex salts. It and many of its derivatives enter into stable molecular combinations with picric and picrolonic acids, and since the products which are formed in this way are relatively insoluble, crystallize well, and possess in most cases sharp melting points, they frequently serve for purpose of identification.

The structural formula in common usage at the present time is not the hexagonal form that was suggested by Pinner, but the following expression:



$$\begin{array}{ccc} (1) & \mathrm{N{=}CH} & (6) \\ & |\qquad| & \\ (2) & \mathrm{HC}\quad\mathrm{CH} & (5) \\ & \|\qquad\| & \\ (3) & \mathrm{N{-}CH} & (4) \end{array}$$

in which the position of the component atoms is indicated by numerals. According to this system cytosine would be referred to as 2-oxy-6-aminopyrimidine.[3]



$$\begin{array}{c} \mathrm{N{=}CNH_2} \\ |\qquad| \\ \mathrm{OC}\quad\mathrm{CH} \\ |\qquad\| \\ \mathrm{HN{-}CH} \end{array}$$

This arrangement possesses an obvious advantage over the hexagonal form because of the fact that it serves to emphasize the existence of the urea grouping in the pyrimidine molecule. Since many derivatives of pyrimidine (such as, for example, uracil) may be synthesized by condensing ureas, sulfur ureas, or guanidines with different β-ketonic esters, this type of formula also presents a graphic method for representing such reactions:

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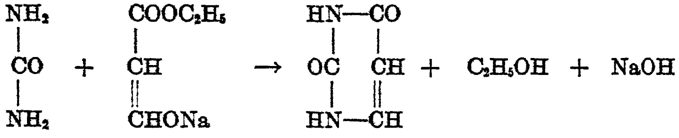
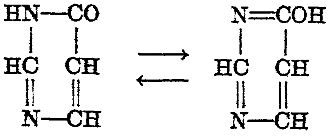
[3] According to the Geneva nomenclature, however, cytosine would be described as 4-amino-2-pyrimidone.



Pyrimidine, like pyridine, yields derivatives (as for example, halogen, nitro, and amino substitution products) which result from direct or indirect replacement of the hydrogen atoms of the nucleus. A large number of these derivatives are, however, obtained as the result of special syntheses. So long as no oxygen or sulfur atoms are in direct union with the atoms of the ring, the strongly basic character of the pyrimidine nucleus remains unchanged. With the substitution of even one oxygen atom, however, an amphoteric substance is formed which possesses weakly basic and weakly acidic properties, the latter being due probably to the ionization of hydrogen in the lactim modification:

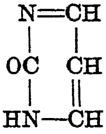


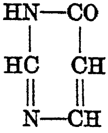
With the introduction of each additional oxygen atom in such positions the acidic properties of the pyrimidine become more pronounced, while its basic properties recede. These changes are so striking that the term "pyrimidine base" becomes exceedingly misleading when applied to these derivatives. It is in fact incorrectly used in referring to the different classes of so-called oxypyrimidines or pyrimidones (Geneva nomenclature).

In classifying the pyrimidines it has seemed desirable, in recognition of these fundamental differences in their properties, to consider special groups in the following order:

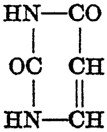
I. True pyrimidine bases. This group includes pyrimidine and its homologues together with their respective halogen, amino, and nitro derivatives.

II. Monoöxypyrimidines. Substances belonging to this group include 2-oxypyrimidine and 6-oxypyrimidine, together with their homologues and other derivatives, any one of which is capable of existing in tautomeric modifications.

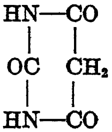

2-Oxypyrimidine


6-Oxypyrimidine

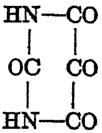
Groups III, IV, and V represent different types of more highly oxygenated pyrimidines:


Uracil

(Group III)


Barbituric acid

(Group IV)


Alloxan

(Group V)

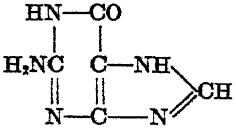
These substances, together with their homologues and other derivatives, are also capable of existing in lactam–lactim modifications.

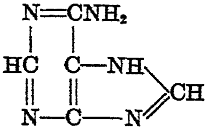
It will be noticed in comparing the above formulas that substances belonging to groups IV and V differ from those in groups I, II, and III, not only as to the position and number of oxygen atoms present in their molecules, but also in the fact that they possess completely saturated ring structures,—the ethylene linkage in the 4,5-position having been eliminated.

Pyrimidines occurring in nucleic acid combinations

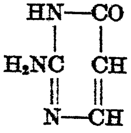
Before undertaking a systematic survey of these different groups of pyrimidines in the order mentioned above, it seems desirable to consider briefly at this point the distinguishing characteristics and also the various tests which have been used in identifying those particular members of the pyrimidine series which occur repeatedly among the degradation products of nucleic acids. Of these cytosine, uracil, 5-methylcytosine, and thymine may be regarded as the most important. Other pyrimidine constructions which may possibly be expected to occur in the mixtures obtained under the experimental conditions of intense hydrolysis in the presence of sulfuric acid are isocytosine and 6-aminopyrimidine and its deaminized derivative, 6-oxypyrimidine.

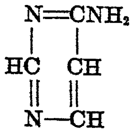
Of the four just mentioned, cytosine, uracil, and thymine occur very widely distributed in nature. Cytosine and uracil are found among the hydrolytic products of both animal and vegetable tissues, while thymine reveals itself in animal tissue only. The question as to whether these substances are to be regarded as primary products actually present as such in the different nucleic acids, or whether they are formed as secondary products, resulting from the hydrolysis of purines, remained an open question for many years. In an attempt to answer it, Richard Burian (27) boiled guanine and adenine,


Guanine


Adenine

in the presence of different carbohydrates with a 30 to 40 per cent solution of sulfuric acid. His results seemed to show that under the conditions of his experiments these purines hydrolyzed to give isocytosine and 6-aminopyrimidine, respectively.


Isocytosine


6-Aminopyrimidine

It therefore seems possible from such evidence that these substances, together with their deaminized derivatives, uracil and 6-oxypyrimidine, may be found along with other pyrimidines among the products formed in the energetic hydrolysis of nucleic acids under the action of sulfuric acid (196a), since guanine and adenine have been identified as occurring in these complex combinations with great frequency. Such a conclusion has, however, been refuted by Kossel and Steudel (124), by Steudel (183), and by Levene and Mandel (140). In spite of the negative experimental evidence brought forward by these investigators, the possibility still remains that with refinements in the technique of separating the pyrimidine fractions from nucleic acids after hydrolysis, and of isolating their components, Burian's conclusions may yet find confirmation. But whether or not pyrimidines will be found under certain conditions to be formed as secondary products of hydrolysis, it has now been demonstrated conclusively that the pyrimidines cytosine, uracil, and thymine are present as such coupled with sugars in nucleic acids.

Of the two aminopyrimidines cytosine and 5-methylcytosine, the former is the only representative which has been shown to be widely disseminated in nature. Cytosine was discovered and named by Kossel and Neumann (121), who separated it in impure condition from the cleavage products of thymus nucleic acid. It was not isolated in pure form until some years later, when it was obtained independently from the testicles of the sturgeon and the herring by Kossel and Steudel (123), and from various animal organs by Levene (130). Convenient methods of preparing it from the thymus, spleen, and pancreas glands have been described by Levene (132a, 133). It has also been found among the hydrolytic products from wheat embryo (158a, 203g) and from yeast nucleic acid (132b, 127).

The structure of cytosine, based on the results of its analysis and the fact that it yields uracil by hydrolysis, was first suggested by Kossel and Steudel (123) and later confirmed by Wheeler and Johnson (203a), who synthesized both cytosine and isocytosine and established the identity of the former with specimens of natural cytosine obtained from the nucleic acids of wheat embryo and from spleen.

Interest in 5-methylcytosine centers at present in the fact that Johnson and Coghill report having isolated and identified it among the products of hydrolysis of tuberculinic acid (91). Tuberculinic acid, obtained from tubercle bacilli, was first studied by Ruppel (172), who stated that it yielded thymine on hydrolysis, although he offered no analytical data to support his conclusions. It was investigated later by Levene (129), who did not, however, succeed in obtaining a pure pyrimidine compound of constant composition. Working with the small quantities of acid at his disposal, his analytical data nevertheless appeared to indicate the presence of a mixture of thymine and uracil in the pyrimidine fraction which he was able to separate from the products of hydrolysis. Johnson and Brown, in continuing this investigation at the request of the Research Committee of the National Tuberculosis Association, were able to report improved methods for preparing proteins from the tubercle bacilli (87) and a convenient method for isolating a tuberculinic acid of constant composition (85). In continuing this work they were able to report the separation and identification of thymine and cytosine from the hydrolytic products which were formed under the action of sulfuric acid. They, therefore, came to the conclusion that tuberculinic acid is a nucleic acid of animal origin; this was later confirmed by the separation of levulinic and formic acids from the sugar fraction in amounts large enough to indicate the presence of a hexose sugar in the tuberculinic acid molecule (23). Whether this sugar will be found to be *d*-desoxyribose, as in the case of thymus nucleic acid, remains to be determined by further investigation.

As a result of their continued investigations, Johnson and Brown were able to show that the purines guanine and adenine were also present along with the pyrimidines mentioned above (86) and that in the process of purifying the nucleic acid, guanine showed a tendency to be split off leaving a trinucleotide molecule. Both guanine and adenine were obtained in amounts sufficient to indicate considerable cleavage of tuberculinic acid during the process of purification.

Still later Johnson and Coghill (91) reported the separation of a third pyrimidine which they identified as 5-methylcytosine. This substance was obtained in the form of its picrate, which was found to agree in all respects with the picrate of synthetic 5-methylcytosine (204a). This work has not been repeated and the structure of 5-methylcytosine therefore depends entirely upon the results of its analysis and its synthesis. The discovery of this pyrimidine among the hydrolytic products of tuberculinic acid requires a revised conception of the configuration of the nucleic acid molecule. It now becomes an open question as to whether thymine is present as such or whether it represents a secondary product formed as the result of the deaminization of 5-methylcytosine. The answer to this question cannot be given until much more exhaustive investigations of tuberculinic acid and other nucleic acids have been completed. Further study of the nucleic acids functioning in bacterial cells will undoubtedly contribute valuable data which will advance our knowledge of this interesting class of biological substances.

Tests for cytosine and uracil, 5-methylcytosine and thymine

Up to the year 1907, the identification of pyrimidines, which were isolated from mixtures resulting from the hydrolysis of nucleic acids, depended upon analyses of the pure substances, further confirmation being obtained as a result of the preparation of their sulfates, chloroplatinates, and picrates or picrolonates in cases where such derivatives showed characteristic features (melting points, crystal form, etc.) and were readily accessible. With the discovery of certain definite color tests for cytosine and uracil by Wheeler and Johnson (205a), a convenient method was introduced by means of which small quantities of these compounds could be detected even when they were impure or actually in mixtures with other substances.

This test consists in treating 5 cc. of an aqueous solution of the substance to be tested with small quantities of bromine water until the red bromine color is permanent. Excess of bromine is to be avoided and may be removed by passing a current of air through the solution. If the substance to be tested is cytosine the solution should be warmed or boiled and then cooled after adding the bromine, but prolonged boiling should be avoided as it interferes with the test. To the cold solution prepared in this way an aqueous solution of barium hydroxide is then added in excess, when a purple or violet-blue precipitate or color is immediately formed. In cases where the solution to be tested is very dilute, it may be evaporated to dryness, taken up in a small quantity of bromine water, and then treated as described above. In this way quantities as small as 0.001 g. of uracil have been found to give a bluish pink or lavender color. Since the presence of picric acid interferes with this test it should be removed before making it.

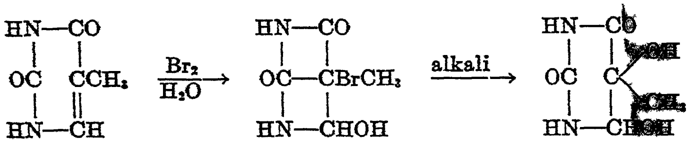
These reactions with bromine water and barium hydroxide involve the transformation of both cytosine and uracil into dibromoöxydihydrouracil and the conversion of the latter into the almost insoluble, purple barium salt of dialuric acid (14b).

A color test that can be used for the detection of either 5-methylcytosine or thymine was discovered by Johnson and Baudisch (84, 9) some fourteen years later. This is somewhat more complicated and consists in dissolving, for example, 2.5 g. of thymine in 200 cc. of hot water in a 5 l. flask and adding first 200 g. of sodium acid carbonate dissolved in 2 l. of water and then 100 g. of freshly prepared ferrous sulfate dissolved in 500 cc. of water. This mixture is shaken violently in a current of air, when a colorless precipitate of iron hydrogen carbonate immediately begins to separate. This precipitate, on shaking, gradually absorbs oxygen from the air with the formation of an unstable peroxide which acts as an oxidizing agent. During a period of one-half to three-quarters of an hour the thymine is gradually oxidized and this is accompanied by a change in the color of the precipitate from white to greenish grey, and then to a brownish color resembling that of ferric hydroxide. When this point is reached the shaking is discontinued and the mixture allowed to stand until the precipitate has completely settled. A portion of the clear supernatant liquid equal to about 100–200 cc. is then evaporated to dryness on a steam bath, when the residue is redissolved and again evaporated. The dry residue is then taken up in a small quantity of water and the indigo test for pyruvic acid applied. This consists in treating 5–10 cc. of solution with a few drops of *o*-nitrobenzaldehyde, adding 1–2 cc. of concentrated potassium hydroxide, and then shaking the mixture with chloroform. The indigo which forms immediately dissolves in the chloroform, giving a characteristic blue solution. The aqueous layer may then be separated and tested for urea with xanthydrol (Fosse's reagent).

The remainder of the original thymine solution is then distilled by boiling over a free flame and the distillate treated with a few drops of *o*-aminobenzaldehyde, when it is again heated to boiling. If acetol is present here the cooled solution will show a characteristic blue fluorescence due to the formation of 3-oxyquinaldine, on being first acidified with hydrochloric acid and then neutralized with sodium acid carbonate. If desired, colorless needles of 3-oxyquinaldine may be obtained by extracting the solution with ether and then removing the ether by evaporation. In this case the Baudisch test for 3-oxyquinaldine may be applied by treating an aqueous alcohol solution of 3-oxyquinaldine with an alcohol solution of iron chloride, when a characteristic deep red complex salt is formed. The presence of sugar interferes with the above method for detecting thymine and should therefore be avoided (33b).

These two tests for cytosine and uracil, and for 5-methylcytosine and thymine, respectively, may be carried out simultaneously if the following procedure is employed (65a): A solution containing a mixture of uracil and thymine is first treated with bromine water according to the method described on p. 205. If cytosine or uracil is present a violet-blue color or precipitate will be formed immediately upon the addition of aqueous barium hydroxide. If the mixture is then subjected to distillation, the presence of thymine in the original solution will be indicated by the appearance of acetol in the distillate. This can be detected by adding sodium hydroxide to the distillate until it is strongly alkaline and then applying the Baudisch test for acetol (6). 5-Methylcytosine can be detected by precipitating as a picrate and then decomposing this salt with mineral acids and finally testing for thymine in the usual manner. As a result of this general procedure all four of these pyrimidines may be tested for in a very few minutes.

The formation of acetol from thymine may be explained by assuming that the first stages of the reaction follow the same general course as has been indicated in the case of cytosine and uracil, giving thymine glycol (8).



Under the continued action of oxidizing agents this glycol is then oxidized and hydrolyzed in a manner similar to that described by Baudisch, with the disruption of the pyrimidine ring and the formation of urea and acetol. This may be formulated as resulting first in the formation of the intermediate aldehyde acid OCH·C(CH_3)OH·COOH which would then lose carbon dioxide to give the aldehyde of lactic acid. The latter on treatment with alkali would then rearrange to form acetol, CH_3COCH_2OH.

Additional data of service in the separation and identification of cytosine (203a, 196e) and 5-methylcytosine (204a) is to be found in the relative solubilities of these two bases in water along with a knowledge of their respective hydrates and characteristic salts with hydrochloric, hydrobromic, and sulfuric acids. A comparative table showing these relationships has been arranged by Johnson and Menge (110b) which may be of considerable interest. As has been stated, these substances all yield uracil and thymine, respectively, on hydrolysis.

The fact that the purines guanine and adenine yield isocytosine and 6-aminopyrimidine when hydrolyzed under certain conditions has already been mentioned (27). This fact, in conjunction with the observations of Johnson and Coghill (91) in their investigation of tuberculinic acid, suggests at least the possibility that both of these substances, together with their deaminized derivatives, uracil and 6-oxypyrimidine, may be formed as secondary products during the intensive hydrolysis of nucleic acids in the presence of sulfuric acid. All four of these substances have been synthesized, isocytosine by Wheeler and Johnson (203d), by Gabriel and Colman (58d), by Traube (190c, 187), and more recently by Hilbert and Johnson (66b); uracil by Fischer and Roeder (46), by Wheeler and Merriam (207a), and later by Wheeler and Liddle (206), by Gabriel and Colman (58a), and by Davidson and Baudisch (32); 6-aminopyrimidine by Buttner (29h), and by Wheeler and Johnson (205d); and 6-oxypyrimidine by Wheeler and Bristol (198g) and by Gabriel (54). It has also been shown that although isocytosine may be hydrolyzed to give uracil, it differs from its isomer, cytosine, in the fact that when treated with bromine water under the same conditions as have been described in the case of cytosine and uracil, it yields a derivative which is not identical with dibromoöxydihydrouracil and which gives an intense blue color when treated with aqueous barium hydroxide. This color is readily distinguished from the purple or violet-blue coloration which is produced by cytosine and uracil under the same conditions, and can be readily identified by the fact that it immediately disappears on the addition of an excess of aqueous barium hydroxide. Because of this peculiarity the production of this color serves as a very delicate test for isocytosine (205b). 6-Aminopyrimidine gives no color reaction when treated with bromine water and aqueous barium hydroxide under the same conditions (205c). Because of the fact that isocytosine, 6-aminopyrimidine, and 6-oxypyrimidine are precipitated by the same general reagents as are used in the precipitation of cytosine and have been observed to adhere obstinately to the latter compound in such precipitates, a comparative table showing the melting points of these free bases together with those of their respective acetyl derivatives, picrates, picrolonates, and salts with hydrochloric and sulfuric acids has been compiled by Wheeler (196g). This may possibly prove of service in connection with future investigations of the nucleic acids and their degradation products.

Since alkylated, and in particular methylated, purines occur in nature, it would be reasonable to conclude that methylated pyrimidines may also occur in natural products (90a). This possibility has acquired a certain added importance through the discovery of a supposed methylaminopyrimidine among the products obtained from the hydrolysis of Japanese *schōyu* (184), and led Johnson and Mackenzie (106b) to undertake a systematic investigation of methylated pyrimidines (97a) and other alkylated derivatives of various types.

The subject is of particular interest because of the fact that the same tests which may be applied in determining the relative position of an alkyl radical in the pyrimidine nucleus, may also be used in attempting to determine the position of the sugar linkage on pyrimidines in nucleosidic combinations. Richard Burian was the first to speculate on this point. The fact that imidazole rings were known to couple with diazonium salts to give colored derivatives led him to think that since the structure of the purine molecule indicates the presence of an imidazole ring, purines might also behave in a similar way when treated with diazobenzenesulfonic acid, except in cases where the reactive hydrogen in the purine had already been substituted. His failure to obtain colored compounds from *N*-7-substituted purines led him to assume that the reason that purine nucleosides also refused to react with diazobenzenesulfonic acid was due to the fact that the *N*-7-position was in such cases occupied by a sugar molecule. These observations of Burian, while not leading to correct conclusions, nevertheless acted as a great stimulus to later investigations involving the use of this reagent.

Thus the application made by Burian of diazobenzenesulfonic acid in the case of purines actually led to its use in attempts to allocate the sugar linkage in pyrimidine nucleosides. In addition to Burian (28), Evans (35), Steudel (182), and Pauly (159a) have contributed to developments in this field. It was not until 1908, however, that a systematic attempt was made by Johnson and Clapp (90e) to investigate the action of diazobenzenesulfonic acid upon a variety of different classes of pyrimidines. The results which they obtained and which are tabulated in a series of comparative tables by Johnson and Clapp, show that thymine, uracil, and cytosine all react with this reagent to give intensely red solutions, the color in every case being due to the formation of a diazo dye (47). Johnson and Clapp were also able to demonstrate that in the case of a relatively large number of other pyrimidines, in which the hydrogen atoms in the *N*-3-positions had not been replaced by substituting groups, red diazo combinations were formed. In cases where no color was produced these investigators were able to prove that the hydrogen atoms in the *N*-3-positions had been replaced. If these observations are of general application it would seem to follow that pyrimidines which give no color reactions when treated with diazobenzene sulfonic acid[4] may now be regarded as already possessing substituting groups in the *N*-3-position.[5] Subsequent experimental evidence has been in harmony with this conclusion. For example, *N*-1-benzyluracil and *N*-1-benzylthymine react with diazobenzenesulfonic acid to give a red color, while the corresponding *N*-3-benzyl derivatives do not (92). This same characteristic behavior has also been observed in investigations dealing with the behavior of various alkyl halides towards uracil and thymine compounds during alkylation experimentations.

This color test with diazobenzenesulfonic acid is more general in its applications than any other test which has yet been investigated and would seem to indicate with considerable accuracy the position of groups substituting on nitrogen in the pyrimidine ring. Other reagents which have been employed with the same general end in view have not proved so convenient nor have they been capable of very extended application. Diazomethane, for example, has frequently been used successfully as a reagent in various types of methylation and a study of its reaction with cytosine, uracil, and thymine was therefore undertaken with a view to applying it later to nucleic acids as a methylating agent (30). It was thought that if nucleic acids could first be methylated and then subsequently hydrolyzed, the position of the sugar linked to the pyrimidine could be determined from the structure of the methylated pyrimidine which was formed as a result of cleavage. The results of preliminary experiments showed that in the case of uracil and thymine methylation proceeded smoothly and resulted in the formation of *N*-1-*N*-3-dimethyl derivatives in both cases. Cytosine, on the other hand, was found to be very resistant to the action of this reagent, and in the methylation of yeast nucleic acid side reactions occurred so that no definite conclusions could be reached.

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[4] Prepared according to the method described by Pauly (159b).

[5] For different methods of procedure in applying this test see Johnson and Clapp (90e).

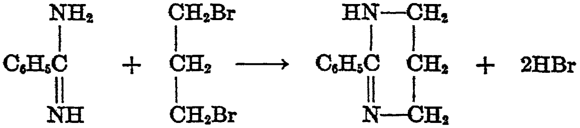
Hydrazine sulfate represents still another reagent which has been applied in attempts to allocate the position of the sugar linkage in nucleic acids. In the single case recorded satisfactory results were obtained. The fact that uracil can be hydrolyzed by this reagent to free urea and formylacetic acid, which then combines with the hydrazine to form pyrazolone (50), formed the basis for this investigation. It was thought that since both urea and pyrazolone give relatively insoluble xanthyl derivatives, it might be possible to obtain corresponding derivatives of either a substituted urea or pyrazolone as the case might be. In applying this test to uridine Levene and Bass (134) obtained the xanthyl derivative of pyrazolone as the only product. This would seem to show that the sugar linkage is on a nitrogen atom of the pyrimidine ring, a conclusion obviously depending upon indirect evidence since a urea pentoside could not be isolated.

In summary, it may be said that the attachment of sugars to the *N*-3-position of the pyrimidine nucleus in nucleosides may be assumed on the basis of the following facts: nucleosides give negative color tests with diazobenzenesulfonic acid; they give negative color tests with bromine water and aqueous barium hydroxide; in one single instance they have been observed to give an unsubstituted pyrazolone under the action of hydrazine sulfate; in a single instance a hexose-pyrimidine nucleoside has been synthesized in which the sugar linkage was definitely determined to be in the *N*-3-position on the pyrimidine (66d). This synthetic nucleoside exhibited the characteristic behavior of the natural nucleoside uridine.

I. PYRIMIDINE HYDROCARBONS, THEIR HOMOLOGUES AND AMINO DERIVATIVES

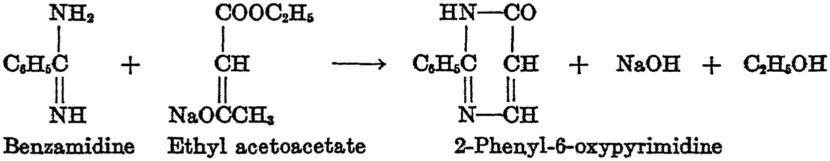
Methods of preparation of pyrimidines and their homologues

Since the reduced pyrimidines may be regarded as derived from formamidine, $NH{=}CH \cdot NH_2$, or substituted amidines having the general formula $NH{=}CR'NHR''$, by the incorporation of these nitrogen linkages into a cyclic structure (194), the first attempts to prepare pyrimidines consisted in an effort to bring about condensations involving ring formation with the synthesis of cyclic guanidines. Only one illustration of direct action resulting in the formation of a cyclic hydrocarbon of this type is recorded in the literature, namely, 2-phenylhydropyrimidine, which was obtained by treating benzamidine with propylene bromide (164a):

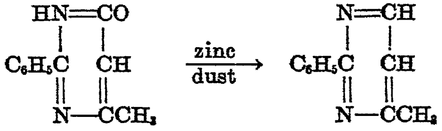


Since this method was not found to be capable of general application, two other methods of somewhat broader scope, but based upon the same general conception, were developed.

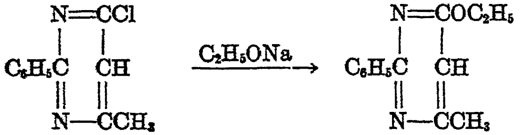
Method I. The first method consists in condensing an amidine in alkaline solution with a β-ketonic ester (161, 162b) as, for example:



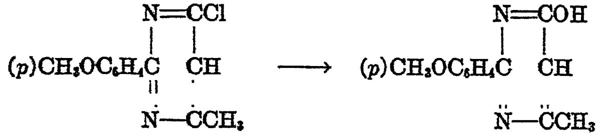
Other amidines which have been found to condense readily with this ketonic ester are $NH{=}C(CH_3)NH_2$, $NH{=}C(C_2H_5)NH_2$, $NH{=}C(C_6H_4OCH_3\text{-}p)NH_2$, and $NH{=}C(C_6H_4NO_2\text{-}p)NH_2$ (162b). The preparation of a pyrimidine hydrocarbon by this method depends for its ultimate success upon the replacement of oxygen in the 6-position of the pyrimidine cycle by hydrogen, but in investigating the condensation products which were obtained in this way Pinner (162b) found that they were extremely stable toward reducing agents and not acted upon by zinc in sodium hydroxide, nor by zinc or tin in hydrochloric acid. In only one case was he actually able to effect reduction, i.e.,



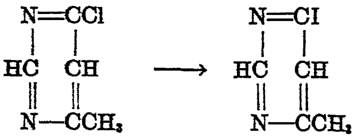
Attempts to overcome this resistance by treating the 6-oxypyrimidine with phosphorus pentachloride or phosphorus oxychloride preliminary to reduction, served to show that chlorine in this position is also very inert toward many of the common reducing agents and that when a reaction takes place it is not always in the sense desired,—sodium and alcohol, for example, reacting to give an oxygen ether:



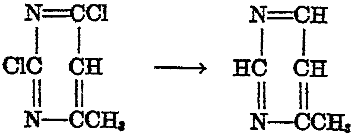
It is of interest in this connection to note that a comparison of the results obtained by treating different 6-chloropyrimidines with different reducing agents under different conditions brings out quite striking differences in behavior. For example, the action of hydrogen iodide and red phosphorus and also of zinc dust and water may result in hydrolysis (55a, 55g, 173c):



The action of hydrogen iodide and red phosphorus may bring about replacement of the chlorine by iodide, as, for example (55x, 29e):

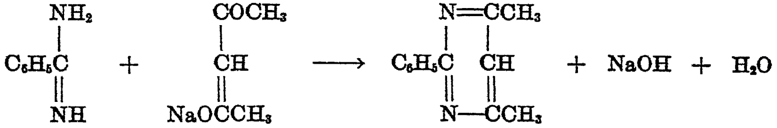


On the other hand, hydrogen iodide and red phosphorus may in certain cases result in replacement by hydrogen (55h):

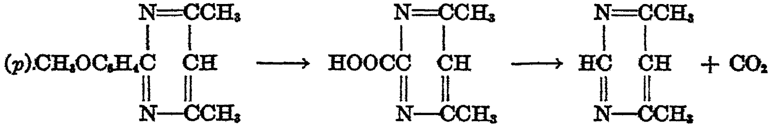


The most dependable results have been obtained by the use of zinc, since reductions with zinc dust and boiling water can almost invariably be relied upon to take place smoothly and to give excellent yields. This applies not only to reductions of chlorine in the 6-position but also in positions 2 and 4 (175c, 55j, 173d). They, therefore, afford in most cases a practical solution of the difficulties that have been experienced in reactions of this type.

Method II. The second condensation referred to above consists in condensing an amidine in alkaline solution with a β-diketone (164c). This condensation also takes place readily with other amidines, as for example, *p*-tolylamidine, $NH{=}C(C_6H_4CH_3)\text{-}NH_2$, benzenylamidine, $NH{=}C(CH_2C_6H_5)NH_2$, β-naphthylamidine, furylamidine (164b), and *p*-methoxybenzamidine, $NH{=}C\text{-}(C_6H_4OCH_3)NH_2$ (55b). In the last case the reaction product was successfully transformed into 2,6-dimethylpyrimidine on oxidation with potassium permanganate and subsequent elimination of a carboxyl group on heating (55c). This method of synthesizing the homologues of the pyrimidine cycle has not received much attention since the researches of the German investigators.



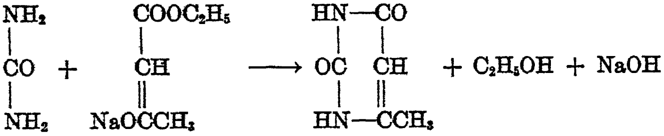
$$\begin{array}{c}NH_2\\ |\\ C_6H_5C\\ \|\\ NH\end{array} + \begin{array}{c}COCH_3\\ |\\ CH\\ \|\\ NaOCCH_3\end{array} \longrightarrow \begin{array}{c}N{=}CCH_3\\ |\qquad |\\ C_6H_5C\quad CH\\ \|\qquad \|\\ N{-}CCH_3\end{array} + NaOH + H_2O$$



$$\begin{array}{c}N{=}CCH_3\\ |\qquad |\\ (p)CH_3OC_6H_4C\quad CH\\ \|\qquad \|\\ N{-}CCH_3\end{array} \longrightarrow \begin{array}{c}N{=}CCH_3\\ |\qquad |\\ HOOCC\quad CH\\ \|\qquad \|\\ N{-}CCH_3\end{array} \longrightarrow \begin{array}{c}N{=}CCH_3\\ |\qquad |\\ HC\quad CH\\ \|\qquad \|\\ N{-}CCH_3\end{array} + CO_2$$

It should be noted, however, in this connection that the action of potassium permanganate has also been observed to result in a cleavage of the pyrimidine ring structure as, for example, in the case of 2-phenyl-4-methyl-6-oxypyrimidine which under these conditions yields benzamidine (162b).

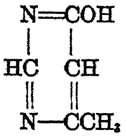
The substitution of the urea grouping for the guanidine grouping in condensations with β-ketonic esters and β-diketones has further extended the scope of this general method for the synthesis of pyrimidines (10b). For example,



$$\begin{array}{c} \mathrm{NH_2} \\ | \\ \mathrm{CO} \\ | \\ \mathrm{NH_2} \end{array} + \begin{array}{c} \mathrm{COOC_2H_5} \\ | \\ \mathrm{CH} \\ \| \\ \mathrm{NaOCCH_3} \end{array} \longrightarrow \begin{array}{ccc} \mathrm{HN} & — & \mathrm{CO} \\ | & & | \\ \mathrm{OC} & & \mathrm{CH} \\ | & & \| \\ \mathrm{HN} & — & \mathrm{CCH_3} \end{array} + \mathrm{C_2H_5OH} + \mathrm{NaOH}$$

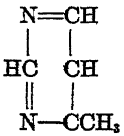
4-Methyluracil

While condensations of this type take place readily they also depend for their ultimate success in the synthesis of reduced pyrimidines upon the subsequent replacement of oxygen by hydrogen in the condensation products. Here again replacement by chlorine is always preliminary to reduction, and is brought about in the usual way under the action of phosphorus pentachloride or the oxychloride. These chlorination reactions take place readily and in excellent yields and a study of the behavior of the resulting 2,6-dichloropyrimidines towards reducing agents has opened up a practical approach to the synthesis of reduced pyrimidines. The investigation of these 2,6-dihalogenated pyrimidines has revealed in several cases a remarkable variation in the behavior of the chlorine atoms occupying these two positions toward reagents other than zinc dust and water. For example, when 2,6-dichloro-4-methylpyrimidine is treated with hydrogen iodide (sp. gr. 1.7) and red phosphorus it reacts to give 4-methyl-6-oxypyrimidine (I); while on the other hand, when treated with fuming hydrogen iodide and red phosphorus or with zinc dust and boiling water it is completely·reduced to 4-methylpyrimidine (II) (55e).



$$\begin{array}{ccc} \mathrm{N} & = & \mathrm{COH} \\ | & & | \\ \mathrm{HC} & & \mathrm{CH} \\ \| & & \| \\ \mathrm{N} & — & \mathrm{CCH_3} \end{array}$$

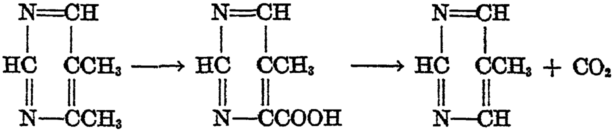
I



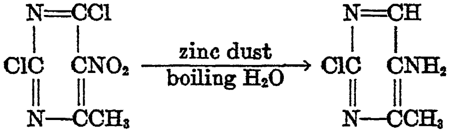
$$\begin{array}{ccc} \mathrm{N} & = & \mathrm{CH} \\ | & & | \\ \mathrm{HC} & & \mathrm{CH} \\ \| & & | \\ \mathrm{N} & — & \mathrm{CCH_3} \end{array}$$

II

A similar difference in the behavior of 2,6-dichloro-4,5-dimethylpyrimidine has been observed under the action of the same reagents (173c). It is interesting to note that 4,5-dimethylpyrimidine, which is formed on complete reduction, yields 5-methylpyrimidine when oxidized with permanganate and then heated to eliminate carbon dioxide from the carboxylic acid formed by oxidation (173e).



The fact that in the reduction of halogen derivatives of the pyrimidines the character of the reduction product depends not only upon the reagent employed but also upon the nature of the other groups present in the molecule is shown by the following reaction (56h),

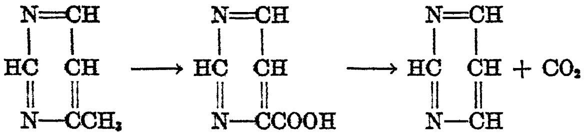


where it is to be noted that the chlorine atom in the 2-position remains unaffected, although it is usually very susceptible to the action of a number of different reducing agents. A similar illustration is to be found in the fact that 2-amino-6-chloropyrimidine is readily reduced, while 2-chloro-6-aminopyrimidine appears to be completely inert, when a mixture of these two isomeric compounds is subjected to the action of zinc dust and boiling water (196b).

In the preparation of pyrimidine hydrocarbons by condensing urea with diketones the primary product consists of a 2-oxypyrimidine which readily lends itself to reduction. Thus, for example, urea and acetylacetone in alkaline solution condense to give 2-oxy-4,6-dimethylpyrimidine (35, 62). This reacts with phosphorus oxychloride in the usual way and the product on treatment with zinc dust and boiling water yields 4,6-dimethylpyrimidine (55d, 181c).

Pyrimidine, the parent substance of this series, may be synthesized in either of the following ways:

(I) Urea condensed with ethyl acetoacetate gives 2,6-dioxy-4-methylpyrimidine, which, as has been stated, may be reduced to 4-methylpyrimidine (55i). The latter on oxidation with potassium permanganate and subsequent heating to eliminate carbon dioxide yields pyrimidine (55l).

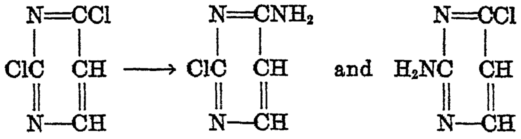


(II) This method differs from any thus far described in that barbituric acid (60, 61, 150, 193, 59, 180b, 22) is made the starting point in the preparation. This pyrimidine is digested with phosphorus oxychloride at 130–140°C. and the reaction mixture then distilled in a vacuum, when 2,4,6-trichloropyrimidine is obtained in yields approximately 80 per cent of theory (51a, 59, 29a). The latter pyrimidine, on reduction with zinc dust and boiling water, gives a 25 per cent yield of pyrimidine (51a).

Methods of preparation of amino derivatives of pyrimidine and its homologues

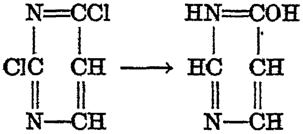
With very few exceptions amino, diamino, and other more highly aminized derivatives of pyrimidine have been prepared either from uracil and its homologues or from barbituric acid by first replacing the oxygen present in these compounds with chlorine, under the action of phosphorus pentachloride or oxychloride, and then treating the product with alcoholic ammonia. In some cases the oxychloride has been found to possess decided advantages over the pentachloride, reacting more readily and giving better yields of the reaction product. In order to obtain a clearer conception of the special methods by which substances belonging to this general class have been synthesized, it seems desirable by way of an introduction to review briefly the principal groups of chloro- and chloroaminopyrimidines which have up to the present time been prepared and studied.

Uracil reacts with phosphorus oxychloride to give 2,6-dichloropyrimidine (III). Care should be taken in handling this substance, since it has a very corrosive action and causes painful blisters (54). The same product may be obtained from 2-thiouracil (110c, 54) under the action of phosphorus pentachloride (205c). The dichloropyrimidine then reacts with alcoholic ammonia to give a mixture of 2-chloro-6-aminopyrimidine (IV) and 2-amino-6-chloropyrimidine (V) (205c, 196b, 54).

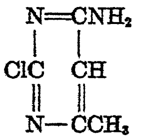


III IV V

On boiling this mixture with water and zinc dust the 2-amino-6-chloropyrimidine (V) is reduced to 2-aminopyrimidine, which is very soluble and can, therefore, be readily separated from the 2-chloro-6-aminopyrimidine which remains unchanged (196b). It may also be noted in this connection that 2,6-dichloropyrimidine behaves quite differently in the presence of hydrogen iodide and red phosphorus. In this case the chlorine in the 2-position is reduced while that in the 6-position is hydrolyzed (196d, 104a):

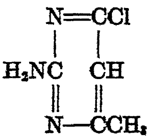


4-Methyluracil (14a) dissolves readily in phosphorus oxychloride on warming to give 2,6-dichloro-4-methylpyrimidine, and the latter when treated with alcoholic ammonia at 100°C. gives the following mixture (VI and VII):



m.p. 218°

VI

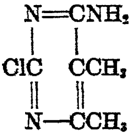


m.p. 181–2°

VII

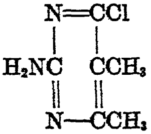
The second of these two isomers (VII) is identical with a substance obtained by treating Jaeger's 2-amino-6-oxy-4-methylpyrimidine (67a, 15b) with phosphorus oxychloride, and in this way its constitution was established (55f, m). The separation of the two isomers (VI and VII) depends upon the fact that 2-amino-6-chloro-4-methylpyrimidine is soluble in benzene and may therefore be removed by extraction (56a).

4,5-Dimethyluracil (10a, 173a) reacts with phosphorus oxychloride to give 4,5-dimethyl-2,6-dichloropyrimidine, and this on treatment with alcoholic ammonia at 100°C. gives (173j) a mixture of VIII and IX.



m.p. 215°

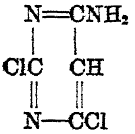
VIII



m.p. 182°

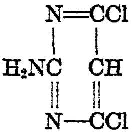
IX

Barbituric acid[6] is insoluble in phosphorus oxychloride but when heated in a sealed tube at 130–140°C. it reacts to give 2,4,6-trichloropyrimidine (51b, 52b, 53, 29c). In the presence of alcoholic ammonia this substance exhibits a marked difference in behavior at different temperatures, one halogen atom only being replaced at 100°C., two at 160°C., and all three at temperatures above 300°C. The product obtained at ordinary temperatures (i.e., up to 100°C.) consists of a mixture of X and XI.



m.p. 271°

X



m.p. 221°

XI

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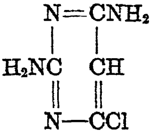
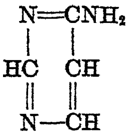
[6] See reference 59 for improved method yielding 80 per cent of theory, and for a complete bibliography of previous methods.

The second isomer is soluble in benzene and may therefore be removed by extraction. Its structure is known from the fact that it may be prepared by treating malonylguanidine with phosphorus oxychloride (29d). On further treatment with alcoholic ammonia both isomers yield the same 2,6-diamino-4-chloropyrimidine and this fact serves as additional evidence in confirming the structural formulas given above. 2,6-Diamino-4-chloropyrimidine

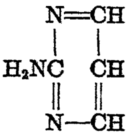


on reduction with zinc dust and boiling water yields 2,6-diaminopyrimidine. 2,4-Chloro-6-aminopyrimidine yields 6-aminopyrimidine with the same reagents, and under the action of other reagents a variety of different products may be obtained. The other chloroaminopyrimidines mentioned previously react in the same way, so that these different classes of compounds may be used as starting points for the preparation of a relatively large number of substances.

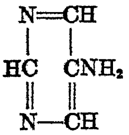
Since aminopyrimidines existing in two isomeric modifications (XII and XIII) are available by the above methods of synthesis, it has seemed desirable to consider in two separate classes all substances which may be regarded as derived from one or the other of these two forms. It will not be possible to mention the salts, picrates, etc., in the case of all of these substances, but literature references will supply these omissions. A third class derived from 5-aminopyrimidine (XIV) as the mother substance may also be noted in this connection, since it will be considered in some detail later in the text.



XII

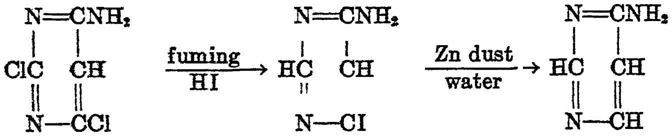


XIII

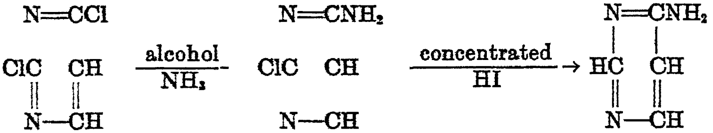


XIV

6-Aminopyrimidine (XII) has already been referred to as resulting from the intensive hydrolysis of the purine adenine. It may be synthesized in the following way (29h),



or as follows (205c, 196c, 104a):



6-Amino- and 6-anilino-4-methylpyrimidine may be prepared (a) by reducing 2-chloro-4-methyl-6-aminopyrimidine and 2-chloro-4-methyl-6-anilinopyrimidine, respectively, with zinc dust and water (56a), or (b) by treating 6-chloro-4-methylpyrimidine with alcoholic ammonia and with aniline, respectively (55v). 2-Amino-4-methylpyrimidine may also be obtained by reducing 2-chloro-4-methyl-6-aminopyrimidine with zinc dust and water (55s). A nitroamino derivative of this pyrimidine is formed as a result of nitration (56d).

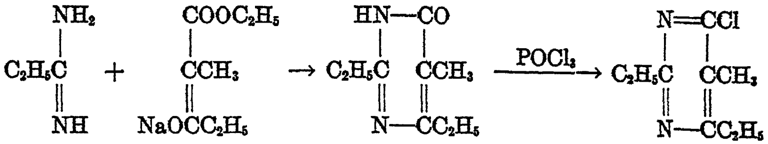
6-Amino- and 6-anilino-2-phenyl-4-methylpyrimidine result from treating the corresponding 6-chloro derivatives in the above way (163, 162b).

6-Amino- and 6-anilino-2-p-tolyl-4-methylpyrimidine have been prepared from the corresponding 6-chloro derivatives by heating with alcoholic ammonia at 180–190°C. and with aniline in benzene, respectively (116d).

6-Amino- and 6-anilino-2,4-dimethylpyrimidine result from treating the corresponding 6-chloropyrimidines with alcoholic ammonia (175c, 178, 106a) and with aniline, respectively (175d).

6-Amino- and 6-anilino-4,5-dimethylpyrimidine may be prepared respectively from 2-chloro-4,5-dimethyl-6-aminopyrimidine and the corresponding 6-anilinopyrimidine by reduction with zinc dust and water (173l).

6-Amino- and 6-anilino-2,4-diethyl-5-methylpyrimidine may be synthesized in the following way:

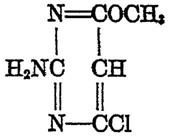


$$\begin{array}{c}NH_2\\ |\\ C_2H_5C\\ \|\\ NH\end{array} + \begin{array}{c}COOC_2H_5\\ |\\ CCH_3\\ \|\\ NaOCC_2H_5\end{array} \rightarrow \begin{array}{ccc}HN & — & CO\\ | & & |\\ C_2H_5C & & CCH_3\\ \| & & \|\\ N & — & CC_2H_5\end{array} \xrightarrow{POCl_3} \begin{array}{ccc}N & = & CCl\\ | & & |\\ C_2H_5C & & CCH_3\\ \| & & \|\\ N & — & CC_2H_5\end{array}$$

Ethyl
propionylpropionate

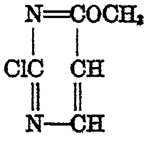
The chlorination product is then treated with alcoholic ammonia and aniline, respectively (148).

2-Aminopyrimidine (XIII), like its isomer 6-aminopyrimidine, may be obtained in either of two ways: (a) from barbituric acid by passing to 2,4,6-trichloropyrimidine, and then to 2-amino-4,-6-dichloropyrimidine, the latter being reduced under the action of zinc dust and boiling water (29d). It should be noted in this connection that attempts to reduce 2-amino-4,6-dichloropyrimidine with sodium in methyl alcohol resulted in the formation of the oxygen ether,



$$\begin{array}{ccc}N & = & COCH_3\\ | & & |\\ H_2NC & & CH\\ \| & & \|\\ N & — & CCl\end{array}$$

This on subsequent treatment with zinc dust and boiling water yields 2-aminopyrimidine as the final product (52a). (b) From uracil by passing to 2,6-dichloropyrimidine and then to 2-amino-6-chloropyrimidine, the latter being reduced with zinc dust and boiling water (104a). A modification of this procedure consists in treating 2,6-dichloropyrimidine with sodium methylate. The product consists of the methyl ether,



$$\begin{array}{ccc}N & = & COCH_3\\ | & & |\\ ClC & & CH\\ \| & & \|\\ N & — & CH\end{array}$$

which may be transformed into 2-aminopyrimidine by treating it first with alcoholic ammonia and then reducing the methoxy group under the action of zinc dust and hydrogen chloride in absolute alcohol (58c).

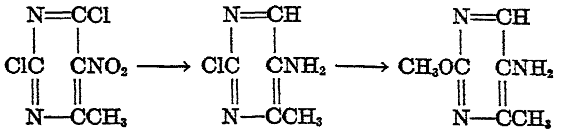
A 2-anilinopyrimidine corresponding to the above may be prepared by the synthesis of 2-phenylanilino-6-oxypyrimidine and its subsequent treatment first with phosphorus oxychloride and then with zinc dust and water (98a).

2-Amino-4-methylpyrimidine may be prepared from 4-methyluracil by passing to the corresponding 2,6-dichloro derivative and then to 2-amino-6-chloro-4-methylpyrimidine, reduction being effected in the usual way (55p). It may also be prepared from Jaeger's 2-amino-4-methyl-6-oxypyrimidine (67a, 15a) by treating with phosphorus oxychloride in the usual way and then reducing with zinc dust (55p).

2-Amino-4,5-dimethylpyrimidine may be obtained from 4,5-dimethyluracil (10a) by passing first to the corresponding 2,6-dichloro derivative and then to 2-amino-6-chloro-4,5-dimethylpyrimidine (173j). The latter is identical with the compound obtained by condensing guanidine with ethyl acetopropionate and treating the condensation product with phosphorus oxychloride (173f). The 2-amino-6-chloro-4,5-dimethylpyrimidine which is formed in either of these two ways is reduced smoothly by zinc dust and water (173i).

2-Amino-4,6-dimethylpyrimidine may be obtained from 2-oxy-4,6-dimethylpyrimidine (35) by treatment with phosphorus oxychloride and then with alcoholic ammonia in the usual way (181e). When aniline is used in place of ammonia, the corresponding 2-anilino derivative is formed.

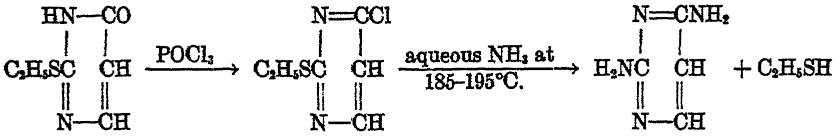
Only one member of the class of monoaminopyrimidines in which the amino group occupies the 5-position has as yet been described in the literature. This is *4-methyl-5-aminopyrimidine* and is prepared by the application of an entirely different method of procedure in that it is formed by the direct reduction of a nitro group in the 5-position of the pyrimidine ring. For example, 2,6-dichloro-4-methylpyrimidine yields on nitration a corresponding 5-nitro derivative (56e). This on reduction with zinc dust and subsequent treatment with sodium methylate undergoes the following transformations,



and the product when treated with fuming hydrogen iodide and phosphonium iodide yields 4-methyl-5-aminopyrimidine.

Relatively few diaminopyrimidines have been prepared and studied. The substances investigated have been synthesized by methods closely analogous to those developed in the preparation of the monoaminopyrimidines,—having in most instances been obtained as transition products either from the 2,6-dihalogen derivatives of uracil and 4,5-dimethyluracil, or from the 2,4,6-trihalogen derivative of barbituric acid. Other general methods for the preparation of 2,6-diaminopyrimidines involve (a) the synthesis of 2-amino-6-oxypyrimidines by condensing guanidine with β-ketonic esters, followed by the conversion of these 6-oxy condensation products into their respective 6-chloro and then into 6-amino derivatives by application of the usual methods; (b) the synthesis of 2-mercapto-6-oxypyrimidines by condensing pseudothioureas with β-ketonic esters, followed by the conversion of the condensation products into the corresponding 2-amino or 2-anilino derivatives with subsequent replacement of oxygen in the 6-position by one or the other of these or similar groups.

Diaminopyrimidines which contain amino groups in the 5-position of the ring are prepared by special methods which involve at some point in the procedure the reduction of a nitro or a nitroso group in this position. *2,6-Diaminopyrimidine* may be obtained from 2,6-diamino-4-chloropyrimidine (29a) by treating it first with hydrogen iodide and red phosphorus and then reducing the resulting 2,6-diamino-4-iodo derivative with zinc dust and water (29i). The same substance may also be prepared by starting with 2-ethylmercapto-6-oxypyrimidine as represented below (203c, 100a).



2,6-Dianilidopyrimidine was obtained from 2-ethylmercapto-6-chloropyrimidine by heating with two molecular proportions of aniline at 150°C. (100c).

2,6-Diamino-5-carbethoxypyrimidine was prepared from the corresponding 2-ethylmercapto-5-carbethoxy-6-chloropyrimidine in a similar way (200b).

2-o-Toluidino-6-amino- and 2-p-toluidino-6-anilido-pyrimidine have been obtained by starting with 2-ethylmercapto-6-oxypyrimidine and treating it with *o*- and *p*-toluidine, respectively. The products obtained in this way were treated first with phosphorus oxychloride and then with alcoholic ammonia at 140–150°C. or with aniline in benzene solution, respectively. The corresponding 2-*o*-toluidino-6-anilidopyrimidine was obtained by warming the corresponding 6-chloro derivative with aniline in benzene solution (116c).

2,6-Diamino-4-methylpyrimidine was prepared from the corresponding 2,6-dichloro-4-methylpyrimidine (56j) and also from 2-amino-4-methyl-6-oxypyrimidine by the usual methods (55o, 56j).

2,6-Diamino-4-methyl-5-nitropyrimidine was prepared by first nitrating 2,6-dichloro-4-methylpyrimidine and then replacing the chlorine in the usual way (56e).

2-Amino-6-anilino- and 2-anilino-6-amino-4-methylpyrimidine were obtained from 2-amino-6-chloro- and 2-anilino-6-chloro-4-methylpyrimidine by treatment with aniline and alcoholic ammonia respectively (55q).

2,6-Diamino-4,5-dimethylpyrimidine and 2-amino-6-anilino-4,5-dimethylpyrimidine were prepared from 2-amino-6-oxy-4,5-dimethylpyrimidine in the usual way (173g).

2-Anilino-6-amino- and 2,6-dianilino-4,5-dimethylpyrimidine were obtained from the corresponding 2-chloro-6-amino (173k) and 2,6-dichloro (173m) derivatives.

4,6-Diaminopyrimidine was prepared from 4-iodo-6-aminopyrimidine by treatment with alcoholic ammonia (29f).

5,6-Diamino-4-methylpyrimidine was obtained from 2-chloro-4-methyl-5,6-diaminopyrimidine by reduction with hydrogen iodide and red phosphorus (56g), and *2,5-diamino-4-methylpyrimidine* from 2-chloro-4-methyl-5-aminopyrimidine by treatment with alcoholic ammonia (56i).

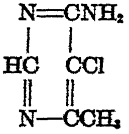
A few more highly aminized pyrimidines have also been prepared and studied. These are: *2,4,6-triaminopyrimidine,* prepared from the corresponding trichloro derivative of barbituric acid (52a) and also from 2-methylmercapto-4,6-dichloropyrimidine (199b). This substance on nitration yielded a 5-nitro derivative which reduced to give *2,4,5,6-tetraaminopyrimidine* (52c). *2,4-Dianilino-6-aminopyrimidine,* prepared from 2-methylmercapto-4-chloro-6-aminopyrimidine by heating with two molecular proportions of aniline at 140–150°C. for ten hours (100e). *2,5,6-Triamino-4-methylpyrimidine,* prepared by nitrating 2,6-diamino-4-methylpyrimidine and then reducing the product with tin and hydrochloric acid (56l).

II. THE PROPERTIES OF PYRIMIDINES AND AMINOPYRIMIDINES

Halogen derivatives

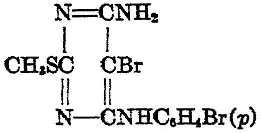
In considering the preparation of pyrimidines and aminopyrimidines from the corresponding halogen derivatives by processes of reduction and aminization, variations in the behavior of halogen in the 2-, 4-, and 6-positions were noted and nothing further needs to be added in this connection.

It remains to be noted, however, that both chlorine and bromine derivatives have been reported in the literature in which the halogen occupies the 5-position in the pyrimidine molecule. Thus for example, 4-methyl-6-aminopyrimidine reacts readily with chlorine in hydrochloric acid solution to give the corresponding 5-chloropyrimidine.



A similar reaction occurs when a molecular quantity of bromine is added to 4-methyl-6-aminopyrimidine (56c) and also to 4-methyl-2,6-diaminopyrimidine (57a) under similar conditions. The halogen in these cases appears to be very firmly seated and to resist replacement by amino groups under the action of alcoholic ammonia (56c).

While mercapto- and thio-pyrimidines have been reserved for special consideration a little later, it may be said in this connection that substances which contain halogen in the 5-position have been reported in the case of 2-mercapto-6-aminopyrimidines and their derivatives. These have been prepared by both direct and indirect methods. For example, *2-methylmercapto-4-chloro-5-bromo-6-aminopyrimidine* and also *2-methylmercapto-4-p-bromoanilido-5-bromo-6-aminopyrimidine*,



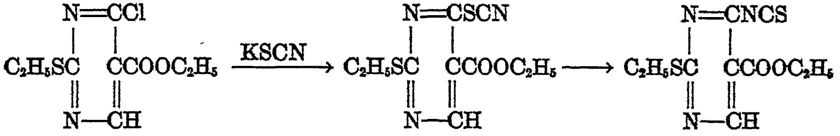
were prepared by dissolving the corresponding unbrominated pyrimidines in acetic acid and adding a molecular quantity of bromine (100d). Under these conditions the product separates in the form of a salt of hydrogen bromide, and the free base is obtained by neutralizing with 10 per cent sodium hydroxide solution. The free base of the second of these compounds was also obtained by the indirect method of heating 2-methylmercapto-4-chloro-5-bromo-6-aminopyrimidine with *p*-bromoaniline. In a similar manner *2-methylmercapto-5-bromo-4,6-diaminopyrimidine* may be prepared by treating the corresponding 4-chloro derivative with aqueous ammonia at 150–160°C. 2-Ethylmercapto-5-bromo-6-aminopyrimidine was obtained by the same indirect method.

Iodine cannot be introduced into the pyrimidine nucleus successfully by direct iodination. It has however been observed to replace chlorine in the 6-position, and also in the 4-position (55u, 34, 29b, 29g). In both positions it is readily reduced by zinc dust and water and readily aminized by alcoholic ammonia at high temperatures.

Amino derivatives

The 2-, 4-, and 6-amino- and anilino-pyrimidines which have been described as being formed from the corresponding halogen derivatives under the action of ammonia or aniline, require specific conditions of temperature and pressure if adequate yields are sought. In the case of 2,4,6-trichloropyrimidine, for example, only one halogen atom is replaced at ordinary temperatures or even up to 100°C., the product consisting of a mixture of 2,4,6- and 4,2,6-aminodichloropyrimidine. At 160°C. a second amino group enters the molecule and 2,4-diamino-6-chloropyrimidine is formed. Finally at temperatures above 200°C. all three chlorine atoms are replaced (52a, 29a). Variations in the behavior of chlorine in different positions toward aqueous and alcoholic ammonia have been frequently reported in the literature (55w, 56b, 58c, 173b, 175a, 181b, 82).

2-Mercapto-6-aminopyrimidines may be prepared indirectly by treating the corresponding 6-chloro derivatives with potassium thiocyanate in toluene and other solvents. For example:

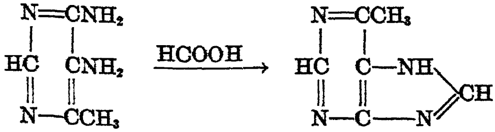


The resulting isothiocyanate when dissolved in absolute alcohol and heated for two hours at 150°C. gave the thionurethane, $\overline{\mathrm{N\cdot C(SC_2H_5){=}N\cdot CH{=}C(COOC_2H_5)C}}\mathrm{\cdot NHCSOC_2H_5}$, and when heated for six hours gave the corresponding 6-amino derivative (88). The structure of the latter substance was confirmed by comparison with a specimen of 2-ethylmercapto-5-carbethoxy-6-aminopyrimidine previously synthesized by Wheeler and Johns (200a).

The corresponding 5-bromo-6-chloropyrimidine also gives an isothiocyanate under the action of potassium thiocyanate and this again may be transformed into the corresponding 6-amino derivative (198d, 108a, 116a).

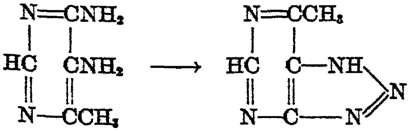
5-Aminopyrimidines cannot be prepared from the corresponding halides, since halogen in this position is not acted upon by aqueous or alcoholic ammonia. They may however be obtained from the corresponding 5-nitro and 5-nitroso compounds by the reducing action of tin and hydrochloric acid (56f, 58e). Substances which contain an amino group in this position can be detected by means of characteristic color reactions. The test is applied by treating the pyrimidine in solution in ammonia under very particular conditions with phosphotungstic acid, when a brilliant blue color is developed (101d, 49, 48, 144).

5,6-Diaminopyrimidine, and also a triaminopyrimidine which possesses this grouping, can be identified by the fact that they are readily transformed into the corresponding purines under the action of different reagents such as formic acid, urea, thiourea, and nitrous acid. For example (56g),



4-Methyl-5,6-diaminopyrimidine 6-Methylpurine

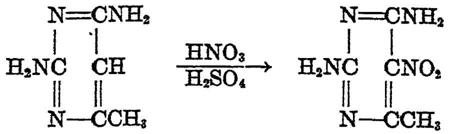
The same diaminopyrimidine, on treatment with urea and thiourea respectively, yields 6-methyl-8-oxypurine and 6-methyl-8-thiopurine, and when its hydrochloride is treated with sodium nitrite in aqueous solution it is transformed into the cyclic diazo derivative or the triazole, azimido-6-methylpyrimidine.



The corresponding 2-chloro-4-methyl-5,6-diaminopyrimidine yields chloromethylpurine when treated with formic acid, 2-amino-4-methyl-5,6-diaminopyrimidine yields 2-amino-6-methylpurine, and 2-thio-4,5,6-triaminopyrimidine when treated in the same way and then desulfurized yields adenine (188b).

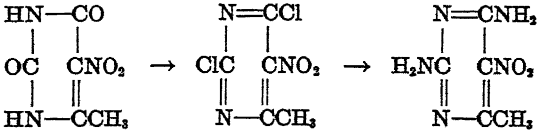
A pentachloropyrimidine, $C_5Cl_5N_2$, has been reported which reacts with alcoholic ammonia to give a monoamino derivative $C_5HCl_4N_2 \cdot NH_2$ (57a). All classes of amino compounds yield the corresponding oxypyrimidine derivatives on treatment with nitrous acid.

5-Nitropyrimidines and aminopyrimidines may be obtained by direct nitration (56k, 52a, 163).

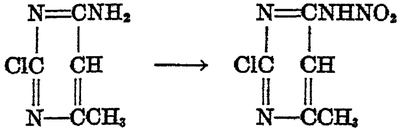


These substances are all reduced under the action of tin and hydrochloric acid to the corresponding amino derivatives.

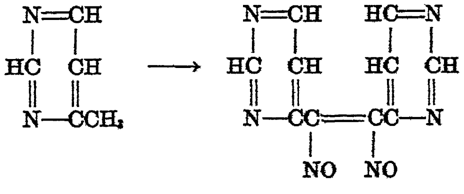
It should be noted, however, that the behavior of pyrimidine and aminopyrimidines under the action of nitric acid varies considerably. This is especially true in the case of aminopyrimidines. Thus, for example, 4-methyl-6-aminopyrimidine and the corresponding 2-chloro derivative yield nitroamines when treated with this reagent (56d).



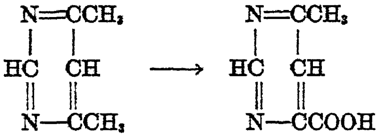
Or, nitro derivatives may be obtained indirectly from the corresponding nitrouracils by the usual method of replacing the oxygen first by chlorine and then by an amino group (56e).



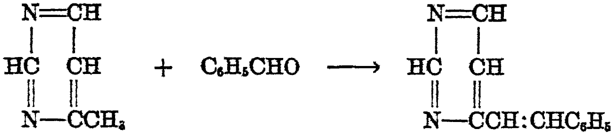
4-Methyl- and 4,6-dimethyl-pyrimidine react still differently, yielding what have been represented structurally as glyoxime superoxides. Very little attention has been paid to the chemistry of these types of nitroso compounds (57b).



4-Methyl- and 4,5-dimethyl-pyrimidine show certain peculiarities of behavior which call for comment, the hydrogen atoms of the methyl group in the 4-position displaying certain of the properties of so-called "reactive hydrogen." Thus, for example, 4-methylpyrimidine is readily oxidized by potassium permanganate to give the corresponding carboxyl derivative (55k). 4,5-Dimethylpyrimidine behaves in a similar manner (173e, 181a).



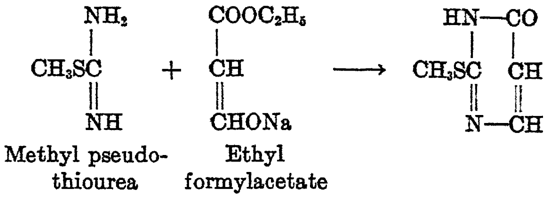
The fact that methyl groups in this position are readily oxidized led to the assumption that they might also be reactive in condensations and this proved to be correct, since 4-methylpyrimidine was found to condense with benzaldehyde in the presence of zinc chloride (58e).



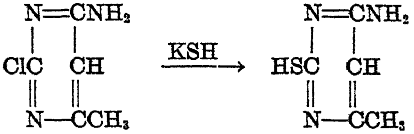
2,4-Dimethylpyrimidine has also been observed to react in the same way (175b). The activity of this hydrogen is probably also responsible for the curious behavior of these substances in the presence of nitric acid. This has already been referred to (57b).

Mercaptopyrimidines

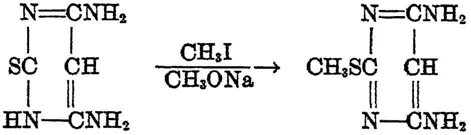
Mercaptoaminopyrimidines have been prepared in which the mercapto group occupies the 2-, 4-, and 6- positions, mono-, di-, and tri-substitution products having been described by different investigators in this field. 2-Mercaptopyrimidines may be obtained synthetically by condensing pseudothioureas with β-ketonic esters and β-diketones (207a).



In this case the corresponding 6-aminopyrimidines can be obtained by means of the usual transformations. 2-Mercaptopyrimidines may also be prepared by the interaction of the corresponding chloropyrimidines with potassium hydrogen sulfide (55t, 181e),



or by alkylating the corresponding thiopyrimidines (188a).



6-Mercaptopyrimidines are prepared exclusively by the second of these three methods (55r, 173h). 2,6-Dimercaptopyrimidines and 2,4,6-trimercaptopyrimidines have been obtained by means of the same general methods (55n, 173n, 29j).

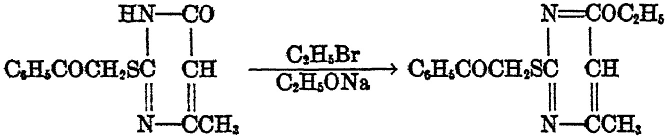
The mercapto groups present in these compounds can usually be hydrolyzed under the action of hydrobromic or hydrochloric acid to give the corresponding oxy derivatives with evolution of mercaptan. They are also replaceable in the 2-position by amino and substituted amino groups (106d, 100b, 98b, 198h, 116b).

The importance attached to the preparation of 2-mercaptopyrimidines by synthetic methods lies in the fact that the presence of this group limits the action of phosphorus oxychloride to the 6-position of the pyrimidine cycle, and this makes possible the preparation of a variety of different derivatives of known structure.

Oxygen ethers

Oxygen ethers in which methoxy and ethoxy groups occupy one or more of the 2-, 4-, and 6-positions in the pyrimidine ring have been prepared from the corresponding halogen derivatives under the action of sodium methoxide and ethoxide, respectively (162b, 55m, 56h, 58b, 173o, 181d, 203d). It should be noted that Buttner in studying the action of sodium methoxide on trichloropyrimidine made the discovery that the formation of mono-, di-, or tri-methoxy derivatives, respectively, was subject to temperature control, the trimethoxy derivative being obtained at 100°C. under pressure (29k).

Ethers of this class have also been obtained by direct alkylation of 2-mercapto-6-oxypyrimidines under the action of alkyl halides in the presence of sodium ethoxide (112).



The same substance gave the corresponding benzyl ether under the action of benzyl chloride. A 2-ethylmercapto-5-ethoxypyrimidine and the corresponding 2,5-diethoxypyrimidine are representatives of a different type which have also been prepared (104b).

Substances belonging to this general class are of considerable interest because many of them tend to undergo rearrangements into the lactam modification. Such transformations belong to

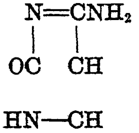
$$\underset{\text{Lactim}}{-\mathrm{N{=}COR}} \rightarrow \underset{\text{Lactam}}{-\mathrm{RN{-}CO}}$$

the type of imido ester rearrangements (117, 118, 202, 195, 95) and in the case of 2,6-dimethoxypyrimidine have led to the discovery of a synthetic method for preparing pyrimidine nucleosides (66c, 81).

III. AMINOÖXYPYRIMIDINES WHICH YIELD URACIL OR ITS DERIVATIVES ON HYDROLYSIS

Monoaminomonoöxypyrimidines

Following the general method of classification outlined in the first chapter of this paper, the amino derivatives of pyrimidine which contain one or more oxygen atoms in union with the carbon atoms of the pyrimidine nucleus, must now be considered. Such substances fall naturally into two groups, (a) those which yield uracil or derivatives of uracil (thymine, etc.) on hydrolysis, and (b) those which yield barbituric acid and its derivatives. The simplest compounds which may be regarded as belonging to the first group are those containing one oxygen and one amino group. Substances having this composition may be accounted for structurally in seven different ways if tautomeric variations in form are disregarded (lactim–lactam modifications) (203b).



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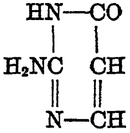

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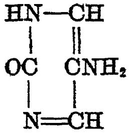

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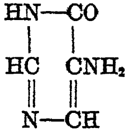

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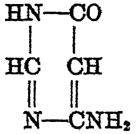

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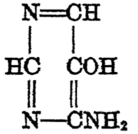

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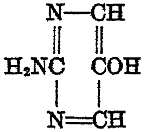


VII

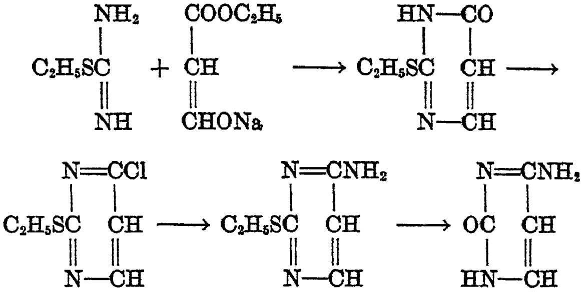
Only the first two of these seven possible molecular configurations could be expected to yield uracil on hydrolysis. These have now been identified as belonging respectively to the two well-known substances, *cytosine* (I) and *isocytosine* (II). Cytosine has been observed to result from the hydrolysis of nucleic acids or other naturally occurring products, but isocytosine has not as yet been found among the degradation products of nucleic acid. Both pyrimidines have been synthesized by methods which admit of no doubt as to their structure. Numerous alkyl and aryl derivatives of each of these two types of substances have also been synthesized, and in every case where the substituting group is not in union with the amino nitrogen atom and is, therefore, not eliminated with it during the process of hydrolysis, such compounds yield corresponding uracil derivatives under the action of hydrolyzing agents. Since cytosine and its derivatives differ from isocytosine and its derivatives both as to their respective methods of synthesis and also as to their properties, the two types of substances will be considered separately.

1. Cytosine

The only *general* method of synthesis which has been found applicable to cytosine and to such of its many possible derivatives as have up until now been investigated, consists in condensing a pseudothiourea with a β-ketonic ester. The product, which contains a mercapto group in the 2-position and an oxygen atom in the 6-position, is treated with a phosphorus halide—phosphorus pentachloride or oxychloride—and then with ammonia in the usual way, and finally desulfurized by warming with mineral acids. In certain cases this procedure has been modified slightly by using thiourea in the initial condensation and then transforming the resulting 2-thio-6-oxypyrimidine into the corresponding 2-mercapto derivative by treatment with metallic sodium dissolved in absolute alcohol. Further transformations of the product obtained in this way follow the general course outlined above. Direct desulfurization, CS → CO, can also be accomplished by digesting a 2-thiopyrimidine with chloroacetic acid. This is a very practical method of operating when the alkylation method is not necessary for the further steps in synthesis.

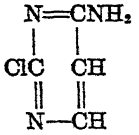
Cytosine was first discovered as a cleavage product of thymus nucleic acid (121) and is very widely distributed in nature, having been obtained from the testicles of sturgeon and herring (123) and from various other animal organs (130, 132a). It has also been found among the hydrolytic products of wheat embryo (158b, 203g) and of yeast cells (132b, 127). The free base has been isolated in the form of its chloroplatinate (123) and of its picrate which was then converted into the sulfate (131). In 1903 the base was transformed into uracil by deaminization with nitrous acid (124).

The structure of cytosine was tentatively suggested by Kossel and Steudel (124), but the first actual synthesis of the substance was accomplished by Wheeler and Johnson (203a). This consisted in condensing ethyl pseudothiourea with ethyl formylacetate in alkaline solution and treating the product first with phosphorus oxychloride, then with alcoholic ammonia, and finally desulfurizing by warming with hydrochloric acid.



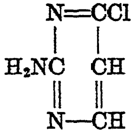
While the technique of this method is difficult for an inexperienced worker, it served for many years as the only practical method for preparing cytosine in quantity. The greatest obstacle in applying this process is to be found in completely eliminating the mercaptan which is evolved during the final hydrolysis without conversion of the resulting cytosine into uracil. Many workers also object to the production of mercaptan odors in laboratory practice.

It is now possible to avoid the use of sulfur compounds in the synthesis of cytosine itself by applying a second special method of procedure which possesses the added advantage of simplifying the operating technique. This consists in starting with 2,6-dichloropyrimidine. The latter is readily prepared from uracil (32) by treatment with phosphorus oxychloride (54). By allowing 2,6-dichloropyrimidine to react with ammonia in alcohol solution at 100°C., Gabriel obtained a mixture of the isomeric chloroaminopyrimidines,



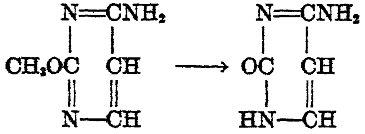
2-Chloro-6-aminopyrimidine

and



2-Amino-6-chloropyrimidine

in the proportions of 40 per cent and 60 per cent, respectively. This mixture may be treated in either of two ways: (a) It may be distilled with steam, when 2-amino-6-chloropyrimidine is removed while its isomer remains behind. The latter can then be hydrolyzed to give cytosine by heating with water at 140°C. The yield is, however, not good because of the fact that some of the 2-chloro-6-aminopyrimidine is transformed into uracil during this process. (b) It may be treated with sodium methylate. In this case a mixture of 2-methoxy-6-aminopyrimidine and 2-amino-6-methoxypyrimidine is obtained without loss of material. The two isomeric ethers may then be separated by recrystallization from hot water in which 2-amino-6-methoxypyrimidine is extremely soluble. In this way yields approximating 40 per cent of 2-methoxy-6-aminopyrimidine may be obtained from 2,6-dichloropyrimidine (66a). When this ether is warmed with dilute hydrochloric acid it passes quantitatively into cytosine without danger of hydrolysis of the latter to uracil.



Cytosine may be readily identified in a number of different ways. It separates from its aqueous solutions with one molecule of water of crystallization, and therefore differs from 5-methyl- and 5-ethyl-cytosine in this respect and also in its solubility in water.[7] Its salts with hydrochloric and sulfuric acids and also its acetyl derivative, picrate, and picrolonate show characteristic properties (196f). Since cytosine is readily hydrolyzed to form uracil it gives a characteristic color test when treated successively with bromine water and barium hydroxide (205a). When oxidized by shaking with air in mixtures of sodium bicarbonate and ferrous sulfate, it gives a characteristic reaction (7). It also gives a red color when treated with diazobenzenesulfonic acid (90g).

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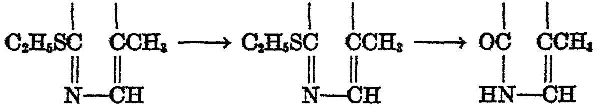
[7] A comparative table showing the relative solubilities of these substances has been compiled (109a).

2. Derivatives of cytosine

Comparatively few of the many possible derivatives of cytosine have as yet been reported in the literature. Of these *5-methylcytosine* is unquestionably the most important. This substance was synthesized by Wheeler and Johnson (204a) as early as 1904, but it was not until 1925 that its presence among the hydrolytic products of tuberculinic acid was discovered by Johnson and Coghill (91). The identity of these two substances was established by means of crystallographic comparison of their respective picrates. Synthetic 5-methylcytosine may be prepared by methods closely analogous to those which have been applied in the synthesis of cytosine. The process consists in preparing 2-ethylmercapto-5-methyl-6-chloropyrimidine by condensing ethylpseudothiourea with the sodium salt of ethyl formylpropionate in alkaline solution and then treating the condensation product with phosphorus oxychloride. The resulting pyrimidine is first purified by distillation under reduced pressure and then heated with alcoholic ammonia for three hours at 127°C. The product is then desulfurized by warming with concentrated hydrochloric acid (204a):



5-Methylcytosine is five times more soluble in water than cytosine and ten to twelve times more soluble than uracil or thymine. It is readily transformed into thymine by heating with 20 per cent sulfuric acid at 150–160°C., or in general by the prolonged action of hot mineral acids. It forms basic salts with halogen acids as, for example, $(C_5H_7ON_3)_2 \cdot HBr \cdot H_2O$. Its picrate has the same solubility in water as that of cytosine; its chloroplatinate is very soluble. It is precipitated by phosphotungstic acid (204a). It gives a negative color test when treated successively with bromine water and barium hydroxide (205a), but yields acetol (65b) when treated successively with bromine water and barium hydroxide under specific conditions. Since it undergoes hydrolysis to give thymine it may be expected to yield acetol, pyruvic acid, and urea when shaken with air in the presence of sodium bicarbonate and ferrous sulfate or other similar oxidation media under well-defined conditions (84). The latter test can be applied in the presence of uracil, cytosine, and also of sugar (33a). 5-Methylcytosine gives an intense red color when treated with diazobenzenesulfonic acid (90h).

5-Ethylcytosine has been synthesized by condensing ethyl pseudothiourea with ethyl formylbutyrate and then treating the condensation product in the usual way (110a). Unlike cytosine and 5-methylcytosine, it separates from its aqueous solutions in an anhydrous condition. It is also distinguished from both of these substances by its solubility in water and by the fact that it is not hydrolyzed by 20 per cent sulfuric acid, the amino group being apparently very firmly seated in the pyrimidine molecule.[8]

Cytosine-5-carboxylic acid and the corresponding *acid amide* have been synthesized by the application of the same general procedure (201, cf. 200a). Other derivatives of cytosine in which the substituents occupy the 5-position are *cytosine-5-acetic acid* (79) and *5-oxycytosine* (109a).

Derivatives of cytosine in which the substituents occupy the 4-position in the pyrimidine molecule have been synthesized in an analogous manner. For example, *4-methylcytosine* is obtained by condensing ethyl acetoacetate with ethyl pseudothiourea in alkaline solution. The product when boiled with phosphorus oxychloride yields 2-ethylmercapto-4-methyl-6-chloropyrimidine, and this when heated in a sealed tube with alcoholic ammonia at 140–150°C. is transformed into the corresponding 6-aminopyrimidine. The latter is readily converted into the hydrochloride of 4-methylcytosine by digesting with concentrated hydrochloric acid. The base is precipitated from the hydrochloride by neutralization of the hydrochloric acid with alkali.

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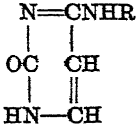
[8] The comparative solubilities of these substances and their respective salts have been determined (110b).

4-Methylcytosine can be readily distinguished from 5-methylcytosine because of the fact that it is far less soluble in water and does not melt at 310°C., while the latter substance effervesces at 270°C. It gives a very characteristic basic hydrochloride containing three molecules of pyrimidine to one molecule of hydrogen chloride. When crystallized from concentrated solutions of the common acids it yields a series of normal salts. Its importance is to be found in the fact that it has been used in the synthesis of certain purine derivatives which will be described later (68).

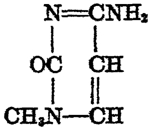
Other interesting derivatives of cytosine which contain substituents in the 4-position are *cytosine-4-aldehyde* (111) and *4-phenylcytosine* (94). In the case of the latter substance the method of preparation was modified, and thiourea was substituted for ethyl pseudothiourea in the condensation with ethyl benzoylacetate. The resulting 2-thio-4-phenyl-6-oxypyrimidine was then transformed into the corresponding 2-ethylmercapto derivative and this into the desired product in the usual way. 4-Phenylcytosine is characterized by the fact that it separates from its solutions in two different crystalline modifications (cf. 99b). *4-Methyl-5-ethylcytosine* has also been prepared by using thiourea in the initial condensation and then proceeding in the manner described above (83c).

Alkylation products of cytosine, 4-methylcytosine, and 5-methylcytosine have been prepared in relatively large numbers, by the application of both direct and indirect methods. Such substances fall naturally into two groups:—those in which the substituent replaces one or more hydrogen atoms of the amino group in the 6-position, and those in which replacement has taken place on the nitrogen atoms occupying the *N*-3-positions in the pyrimidine nucleus, as for example,



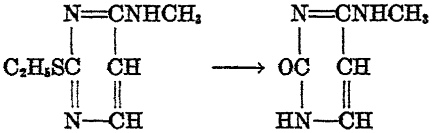
(Group I)

and



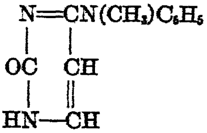
(Group II)

Substances belonging to the first group are usually obtained by treating the corresponding 6-chloropyrimidine with an alkyl or aryl amine but may be prepared by alkylation of the amino nitrogen under the action of an alkyl halide in alkaline solution (198e, 103a, 90a, 72a, 73). Methylated derivatives of cytosine belonging to this group may also be obtained from the corresponding methylated 2-mercaptopyrimidines under the hydrolyzing action of hydrochloric acid:

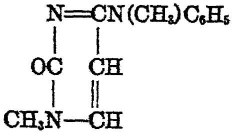


Several examples of this method of preparation have been reported (71, 72b, 74, 76).

Compounds belonging to the second group have been prepared by direct alkylation of cytosine or derivatives of cytosine in alkaline solutions under the action of methyl iodide (90b, 72a, 73). Alkylation products have also been prepared under the action of dimethyl sulfate (75, 77). The presence of substituents in the *N*-3-position of the pyrimidine ring may be detected by the fact that substituting groups in this position inhibits the action of diazobenzenesulfonic acid and negative color tests result. The formation of a red color with this reagent is not, however, dependent upon the presence of a free amino radical in the 6-position in the case of either cytosine or 5-methylcytosine. Thus, for example,

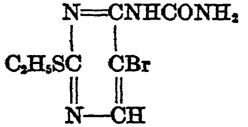


gives a red color with diazobenzenesulfonic acid, while



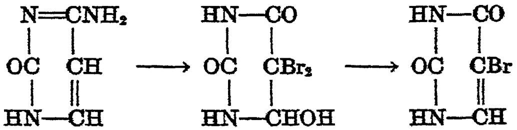
shows no change under the same conditions (90f). This reaction may be of possible significance in allocating the sugar linkage on the pyrimidine molecule in nucleic acid combinations. It is also interesting to note in this connection that the introduction of methyl groups into the cytosine molecule increases the solubility and lowers the melting point of the product (90c).

The number of halogen derivatives of cytosine which have been investigated up to the present time is extremely limited. *5-Bromocytosine* has been prepared by treating 2-ethylmercapto-6-oxypyrimidine dissolved in acetic acid with a molecular quantity of bromine. The resulting product was converted first into 2-ethylmercapto-5-bromo-6-chloropyrimidine, the chlorine replaced by an amino group and the mercapto radical then removed by boiling with concentrated hydrochloric acid (204c). The same substance was also obtained from 2-ethylmercapto-5-bromo-6-ureapyrimidine,



by boiling with concentrated hydrochloric acid (198f).

In studying the behavior of cytosine under the direct action of bromine water, Wheeler and Johnson (203d, 205a) found that the primary product consisted of oxydibromohydrouracil. This on digestion with alcohol was converted quantitatively into 5-bromouracil:



3-Methylcytosine has since been observed to behave in the same way under the action of bromine water, yielding 3-methyl-5-bromouracil (90d). 3,5-Dimethylcytosine yields 3-methylthymine under the same conditions.

5-Iodocytosine is prepared by dissolving synthetic cytosine in dilute aqueous potassium hydroxide and adding finely powdered iodine (102b). *4-Chlorocytosine* is prepared by treating 2-ethylmercapto-4,6-dichloropyrimidine with alcoholic ammonia and then desulfurizing by boiling with concentrated hydrochloric acid (199b). *4-Chloro-5-bromocytosine* was obtained in the form of its hydrobromic acid salt by suspending 4-chlorocytosine in glacial acetic acid and adding a molecular quantity of bromine. The free base was separated by first warming the salt with dilute, aqueous sodium hydroxide and then neutralizing the solution with dilute acetic acid (100f).

It is to be noted that chlorine in the 4-position of certain pyrimidines and also both bromine and iodine in the 5-position are extremely inert and cannot be replaced by an amino group on treatment with aqueous or alcoholic ammonia. Chlorine in the 4-position was not reduced by tin and hydrochloric acid, nor by hydrogen iodide and red phosphorus (199c). Iodine in the 5-position of cytosine behaves in a remarkable way when treated with alcoholic ammonia, being reduced practically quantitatively to cytosine (102a).

A number of different derivatives of cytosine have been prepared which contain a nitro group in the 5-position. Substances of this type command considerable interest because of the fact that they yield 2-oxy-4,5-diaminopyrimidines on reduction, since the latter have been used extensively in the synthesis of the purines.

5-Nitrocytosine was first obtained by treating cytosine with a mixture of nitric and sulfuric acids (204d). Its structure at that time was assumed to be that of a nitramine. Later it was prepared by dissolving 2-ethylmercapto-6-aminopyrimidine in a mixture of nitric and sulfuric acids, when hydrolysis of the mercapto group took place simultaneously with nitration. The product, which consisted of 5-nitro-6-aminopyrimidine, was found to be identical with the substance previously obtained by nitrating cytosine. Its structure was finally definitely established by heating it under pressure with 20 per cent sulfuric acid, when it was converted into 5-nitrouracil (103b). The product may be readily methylated in the 3-position by treating the potassium salt with methyl iodide (72a).

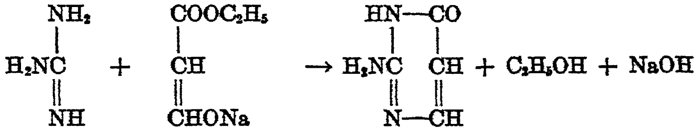
4-Methyl-5-nitrocytosine was obtained in almost quantitative yields when 4-methylcytosine was dissolved in sulfuric acid and then treated with nitric acid (sp. gr. 1.5). The structure of the product was definitely established by heating in a sealed tube with 30 per cent sulfuric acid for two hours at 130–140°C., when 4-methyl-5-nitrouracil was obtained (cf. 13a). The product may be readily methylated in the 3-position by treating with dimethyl sulfate (75).

2-Oxy-5-nitro-6-methylaminopyrimidine was obtained from 7-methylcytosine by dissolving the latter in concentrated sulfuric acid and adding fuming nitric acid to the solution (71). The product may be readily methylated in the 3-position of the ring by treating its potassium salt with methyl iodide (73). *2-Oxy-4-methyl-5-nitro-6-methylaminopyrimidine* was obtained from 2-oxy-4-methyl-6-methylaminopyrimidine in the same way (72c). The corresponding 5-nitro derivatives of 2-oxy-6-ethylaminopyrimidine (76) and of 2-oxy-4-methyl-6-ethylaminopyrimidine (74), were obtained by the use of the same general method.

Cytosine is unacted upon by most reducing agents but under the action of hydrogen in the presence of colloidal palladium the 4,6-ethylene double bond is saturated and it is hydrolyzed smoothly to give hydrouracil as the only product (24b). This behavior is remarkable because it emphasizes the relative instability of the amino group in a reduced pyrimidine nucleus as compared with its very great stability in both the 6- and the 5-positions when ethylene carbon atoms are present in the ring.

3. Isocytosine

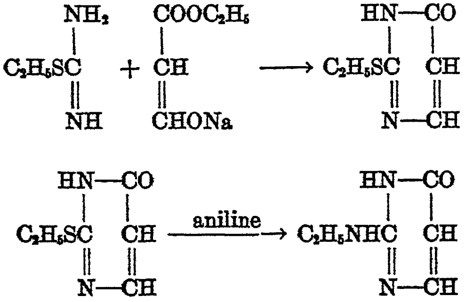
Three general methods have been used successfully for the synthesis of isocytosine and its alkylated derivatives. The first consists in condensing guanidine (203d) with β-ketonic esters in alkaline solutions, as, for example:



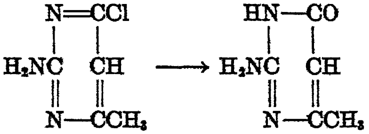
$$\begin{array}{c}NH_2\\ |\\ H_2NC\\ \|\\ NH\end{array} + \begin{array}{c}COOC_2H_5\\ |\\ CH\\ \|\\ CHONa\end{array} \rightarrow \begin{array}{c}HN—CO\\ |\quad\;\; |\\ H_2NC\quad CH\\ \|\quad\;\; \|\\ N—CH\end{array} + C_2H_5OH + NaOH$$

Guanidine Sodium salt of ethyl formylacetate Isocytosine

The second method consists in condensing pseudothioureas with β-ketonic esters and then digesting the product with ammonia, an amine,[9] aniline, etc. (102c).



The third general method consists in the hydrolysis of a halogen atom present in the 6-position of 2-aminopyrimidines (55q):



The above reaction was brought about by the action of hydrogen iodide and red phosphorus, but hydrolysis may be induced by prolonged refluxing with water (66b). In certain cases it has been found convenient to treat the substance with sodium methoxide and then warm the resulting 2-amino-6-methoxypyrimidine with hydrochloric acid (66b).

Isocytosine itself has been prepared by use of the first and third of these general methods (203d, 66b). It has also been prepared independently by the hydrolysis of 2-amino-6-methoxypyrimidine (58c).

4. Derivatives of isocytosine

Derivatives of isocytosine have been described which contain alkyl and aryl groups on the carbon atoms in the 4- and 5-positions in the ring. Such substances have been synthesized by condensing either guanidine carbonate or ethyl pseudothiourea with β-ketonic esters. Another class of derivatives in which the hydrogen of the amino group in the 2-position has been replaced by hydrocarbon residues is also represented by a fairly large number of substances. These have been prepared for the most part by the application of the second general method. Only one derivative containing a substituent in the *N*-1-position has as yet been described.

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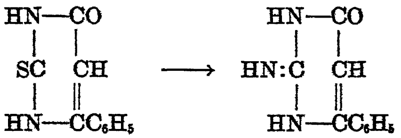
[9] For the use of methylamine in this type of transformation see reference 106e.

4-Methylisocytosine was prepared by condensing guanidine carbonate with ethyl acetoacetate (67a, cf. 15b), and also by treating 2-amino-4-methyl-6-chloropyrimidine with hydrogen iodide and red phosphorus (55o).

5-Methylisocytosine was obtained by condensing guanidine carbonate with ethyl formylpropionate in the presence of barium hydroxide (89a). This substance is characterized by the fact that in the presence of dilute aqueous sodium hydroxide, the pyrimidine ring opens to give a mixture of *cis* and *trans* α-methyl-β-guanidineacrylic acids. Attempts to hydrolyze 5-methylisocytosine to thymine by heating in a sealed tube with concentrated sulfuric acid for five hours were unsuccessful.

4,5-Dimethylisocytosine was prepared by condensing guanidine carbonate with ethyl methylacetoacetate (67c, cf. 173c). This substance hydrolyzes readily in acid solution to give 4,5-dimethyluracil (173c).

4-Phenylisocytosine has been prepared by condensing guanidine carbonate with ethyl benzoylacetate (67d), and also by treating 2-thio-4-phenyl-6-oxypyrimidine with ammonia (191).



The fact that the substance appears to exist in isomeric modifications led to a repetition of Jaeger's experiments by Johnson and Hill (99a).

4-Methyl-5-ethylisocytosine was prepared from 2-ethylmercapto-4-methyl-5-ethyl-6-oxypyrimidine by heating with alcoholic ammonia for three hours at 150–160°C. (83b).

Isocytosine-5-acetamide was prepared by heating the corresponding 2-ethylmercaptopyrimidine with alcoholic ammonia at 170–180°C. for two hours (115).

2-Amino-4-methyl-6-oxypyrimidine-5-acetic acid was prepared by heating the corresponding 2-ethylmercaptopyrimidine with alcoholic ammonia at 170–180°C. for four hours (98f).

5-Ethoxyisocytosine was obtained by condensing guanidine carbonate with the sodium salt of ethyl α-ethoxy-β-oxyacrylate in the presence of barium hydroxide (109b).

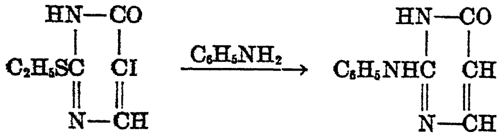
The following substances represent derivatives of isocytosine in which the hydrogen of the amino group in the 2-position has been replaced by alkyl or aryl radicals.

2-Methylamino-5-methyl-6-oxypyrimidine was obtained from the corresponding 2-methylmercaptopyrimidine by treatment with methylamine at 140–150°C. for two hours (106c).

2-Methylamino-4-methyl-6-oxypyrimidine was prepared (a) from the corresponding 2-methylmercaptopyrimidine by treatment with methylamine at 140–150°C. (106e); (b) from 4-methylisocytosine by treatment with methyl iodide in the presence of sodium methylate (67b); and (c) by condensing methylguanidine carbonate with ethyl acetoacetate (146).

2-Methylamino-4-carboxyl-5-methyl-6-oxypyrimidine was obtained from the corresponding 2-ethylmercaptopyrimidine by heating with aniline in alcohol solution (83a).

2-Anilino-6-oxypyrimidine was obtained from 2-ethylmercapto-6-oxypyrimidine by warming with aniline in alcohol solution (102c). It was also prepared by heating 2-ethylmercapto-5-iodo-6-oxypyrimidine with aniline on a steam bath for several hours (102c).



The corresponding 5-bromo derivative was obtained by heating 2-ethylmercapto-5-bromo-6-oxypyrimidine with excess of aniline on a steam bath for several hours. In this case there was no evidence that any reduction of the bromine in the 5-position had taken place during the process (198c).

N-1-Methyl-2-anilino-6-oxypyrimidine[10] was prepared by treating 2-anilino-6-oxypyrimidine with methyl iodide in the presence of sodium methylate (98c). When formed in this way the substance separates from its solutions with one molecule of water of crystallization. An anhydrous modification of the same substance was obtained by heating *N*-1-methyl-2-ethylmercapto-6-oxypyrimidine with aniline at 100°C. for several hours (98c).

2-Benzalamino-6-oxypyrimidine was prepared by heating isocytosine with benzaldehyde at 160–180°C. for three hours (96).

2-Methylanilino-6-oxypyrimidine was obtained from the corresponding 2-ethylmercaptopyrimidine by heating with methylaniline at 100°C. for fourteen hours (98d).

2-Anilino-5-ethoxy-6-oxypyrimidine was prepared from the corresponding ethylmercaptopyrimidine by heating with aniline on a steam bath for several hours (98e).

None of the alkylated derivatives of isocytosine has been investigated with systematic thoroughness, although isocytosine itself has been studied in some detail. It melts at 276°C. and is precipitated by potassium bismuth iodide, but when dissolved in sulfuric acid it yields a brick-red precipitate with this reagent. It gives the murexide reaction. Its salts with hydrochloric and sulfuric acids are very soluble in water but its picrate and double salts with gold and platinum are not very soluble (203e). When boiled with acetic anhydride it yields 2-acetamino-6-oxypyrimidine (196g).

5-Bromoisocytosine has been prepared by dissolving isocytosine in glacial acetic acid and adding a molecular quantity of bromine (203f). The substance separates in the form of its hydrobromic acid salt under these conditions, but aqueous solutions of this salt yield the free base on treatment with ammonia. In this connection it is interesting to note that although 5-bromoisocytosine possesses both acid and basic properties, and therefore is soluble in aqueous ammonia, it nevertheless separates unaltered from its ammoniacal solutions on boiling off the ammonia. 5-Bromoisocytosine, heated with ammonia at 190–215°C. for six hours, reacts to give 2,5-diamino-6-oxypyrimidine (100i).

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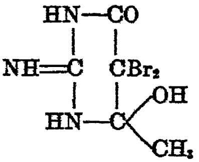
[10] This is the only derivative of isocytosine which has as yet been described that shows replacement of hydrogen in the *N*-1-position.

When isocytosine is treated with bromine in aqueous solution, on the other hand, it behaves quite differently and yields a bromine derivative which, while not identical with the dibromoöxydihydrouracil that is formed when cytosine is treated in this way, gives an intense blue color when barium hydroxide is added to its aqueous solutions. This color is quite readily distinguished from the purple or violet-blue color produced by cytosine or uracil under the same conditions and is further characterized by the fact that it completely disappears when an excess of barium hydroxide has been added. This reaction therefore serves as a delicate test for isocytosine (205b).

5-Bromo-4-methylisocytosine is formed as a secondary product when 4-methylisocytosine is treated with bromine water. The primary product which is formed under these conditions consists of a substance closely analogous to dibromoöxydihydrouracil, viz.:



This when warmed with alcohol yields 2-amino-4-methyl-5-bromo-6-oxypyrimidine. The latter does not react smoothly when treated with ammonia, the product consisting of an oil mixed with small quantities of a crystalline compound. That 4-methyl-5-aminoisocytosine was formed as a result of this action seems probable, however, since the crystalline compound when separated appeared on analysis to have this composition (67a).

5-Nitroisocytosine was prepared by treating isocytosine with a mixture of concentrated sulfuric and nitric acids under special conditions of temperature and concentration (100h). The structure of the product was determined by its conversion into

5-nitrouracil. 5-Nitroisocytosine is readily reduced in ammoniacal solution under the action of aluminum amalgam. Nitrous acid does not react with isocytosine in solution in glacial acetic acid, an acetic acid salt of isocytosine being the only product which was obtained as a result of this treatment (100h).

Isocytosine and methylisocytosine in the form of their silver salts react with acetobromoglucose to give the corresponding tetraacetyl-*d*-glucosides. The latter on deacetylation with ammonia yield the corresponding *d*-glucosides. Both compounds are split by emulsin and takadiastase but not by maltase (63, 64).

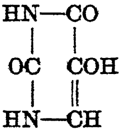
That the amino group in the 2-position is firmly seated would appear from the fact that isocytosine and 4-methylisocytosine both react with phosphorus oxychloride to yield the corresponding 6-chloro derivatives without decomposition. Subsequent replacement of the halogen under the action of different reagents can be effected without involving the amino group (196b, 55m, 173a). The amino group in 2-amino-4,6-dichloropyrimidine seems to be equally stable (29a).

Monoaminodioxypyrimidines

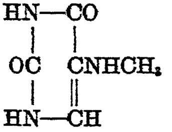
The only monoaminodioxypyrimidines which can be included among the derivatives of uracil contain an amino group in the 5-position, since amino groups in the 2-, 4-, or 6-positions in dioxypyrimidines hydrolyze to give barbituric acid or its derivatives. Very few members of this class of pyrimidines have been investigated up to the present time, the most important being 5-aminouracil and 4-methyl-5-aminouracil. General methods for the preparation of such substances consist (a) in heating the corresponding 5-bromo- or 5-chloro-pyrimidine with ammonia and (b) in reducing the corresponding 5-nitropyrimidine.

5-Aminouracil has been obtained by heating 5-bromouracil (13e, 207b, 204b) with aqueous ammonia. The product was identified by means of its picrate (204b, 16c, 198a). 5-Aminouracil has also been prepared by reducing 5-nitrouracil (119b, 198a, 107b). It should be noted that 5-nitrouracil may be prepared in a number of different ways, viz., by nitrating uracil, 2-ethylmercaptouracil, or 2-thiouracil (198b, 78a, 107a), and also by heating 5-nitrouracil-4-carbonic acid (13b, 16b). The reduction of 5-nitrouracil has been made the subject of extended investigation and can be accomplished more or less successfully under the action of a number of different reducing agents, i.e., with tin and hydrochloric acid (12, 10c), with zinc and hydrochloric acid (13c), with zinc and ammonia (16a), with ferrous sulfate in alkaline solution (209), and with ferrous sulfate and ammonia (107b). A method which appears to afford better yields (70 to 86 per cent) than any of those reported above consists in using aluminum amalgam in the presence of slightly alkaline aqueous ammonia (16b). In all these methods of reduction there is always some formation of isobarbituric acid owing to hydrolysis.

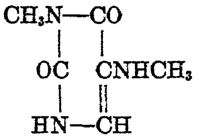
Attempts to bring about reduction catalytically in the presence of colloidal palladium also resulted in a partial hydrolysis of the amino group with the formation of isobarbituric acid (24a).



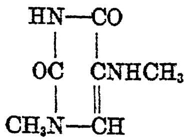
A number of methylated derivatives of 5-aminouracil have been reported in the literature. *1,3-Dimethyl-5-aminouracil* was prepared by treating the potassium salt of 5-aminouracil suspended in methyl alcohol with methyl iodide (107c). The product separated in the form of the salt of hydrogen iodide and the free base was isolated as a secondary product on treatment with silver oxide. *5-Methylaminouracil,*



was obtained by treating 5-bromouracil with methylamine in aqueous solution (207b, 107e). *5-Dimethylaminouracil* was prepared from 5-bromouracil under the action of dimethylamine (199e). *N-1-* and *N-3-methyl-5-methylaminouracil*

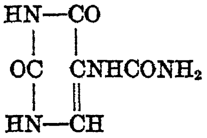


and



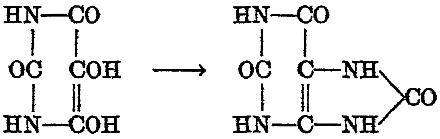
were obtained from the corresponding *N*-1- and *N*-3-methyl derivatives of 5-bromouracil by treatment with methylamine (107d, 97c, 90d).

Various salts of 5-aminouracil have been prepared and described, also its acetyl and benzoyl derivatives (16d). With potassium cyanate it gives pseudouric acid (10d),



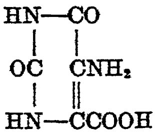
which does not lose water to give a purine but which, like xanthine, is readily oxidized to alloxan (10e; cf. 37).

5-Aminouracil may be transformed into uric acid by a process of simultaneous hydrolysis and oxidation with bromine water and then condensing the product, which consists of isodialuric acid,

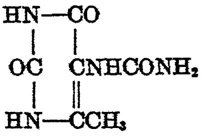


with urea in the presence of sulfuric acid to give a purine by incorporation of an amidazole ring (17).

4-Methyl-5-aminouracil has been prepared from 4-methyl-5-bromouracil (11a) by heating with concentrated aqueous ammonia for several hours. 4-Methyl-5-nitrouracil is easily oxidized to the corresponding nitrouracilcarboxylic acid (13b). The potassium salt of this pyrimidine acid is reduced in aqueous solution by zinc chloride to give *5-aminouracil-4-carbonic acid* (13d, 119a), which is apparently the only pyrimidine aminocarboxylic acid thus far described in the literature.



4-Methyl-5-aminouracil yields an acetyl derivative under the action of acetyl chloride (11d) and reacts with potassium cyanate to give a pseudouric acid (11c).

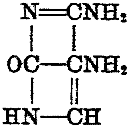


Like the corresponding pseudouric acid obtained from 5-aminouracil, this does not condense to give a purine compound under the action of dehydrating agents.

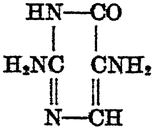
The chemistry of the alkyl derivatives of 4-methyl-5-aminopyrimidine is very incomplete and only one derivative belonging to this class of substances has been reported in the literature. *4-Methyl-5-methylaminouracil* has been prepared by treating 4-methyl-5-bromouracil (11b, 199e) with an excess of aqueous methylamine at 150°C.

Monoöxydiaminopyrimidines

There are five possible monoöxydiaminopyrimidines in which the oxygen atoms occupy the 2- or 6-positions of the pyrimidine ring and in which the amino groups are attached to carbon:



I



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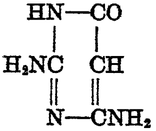
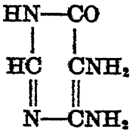
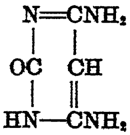


III



IV



V

Of these only the first two can yield uracil or a derivative of this pyrimidine (isobarbituric acid). Both have been synthesized by nitrating cytosine and isocytosine respectively and then transforming the nitro group into an amino group under the action of suitable reducing agents. As has been stated previously in another connection, considerable study has been given to the conditions under which the reduction of a nitro group may be most conveniently effected. In the case of the substances about to be described, aluminum amalgam in the presence of aqueous ammonia or water is used in a number of cases, but in the most recent work this has been replaced by freshly precipitated ferrous hydroxide in aqueous solution, which is recommended as possessing certain distinct advantages.

2-Oxy-5,6-diaminopyrimidine (5-aminocytosine) was obtained by suspending 5-nitrocytosine (204d, 103c) in cold water in contact with aluminum amalgam. The temperature was not allowed to rise above 35°C. during the reduction and the mixture was thoroughly agitated during the 30 minutes required for the reaction. Since the base is characterized by the ease with which it undergoes decomposition in aqueous solution with the evolution of ammonia, the aluminum hydroxide was filtered as rapidly as possible and the clear straw-colored solution evaporated to small volume in an atmosphere of hydrogen under diminished pressure. Under these conditions a crystalline substance mixed with considerable quantities of amorphous flocculent material was deposited. The base crystallizes from its aqueous solution with one molecule of water of crystallization and is quite stable when dry. When dissolved in water it decomposes slowly with the precipitation of amorphous material. Its aqueous solutions are alkaline to turmeric and react with hydrochloric, nitric, and sulfuric acids to form soluble salts. It is an excellent reducing agent, giving a silver mirror when added to an ammoniacal solution of silver nitrate and precipitating the metals from aqueous solutions of gold and platinum chloride. It reduces Fehling's solution instantly. It is precipitated from its aqueous solutions by phosphotungstic acid and by potassio-bismuth iodide (103e).

The reduction of 5-nitrocytosine has also been accomplished under the action of freshly precipitated ferrous hydroxide (70). Because of the marked instability of this substance in the presence of hydrolytic agents and even in solution in water, the possibility of its being identical with "Kutscher's base" is obviously excluded.

2-Oxy-3-methyl-5,6-diaminopyrimidine has been prepared by treating the potassium salt of 5-nitrocytosine in aqueous solution with methyl iodide and then reducing the product with freshly precipitated ferrous hydroxide (72a).

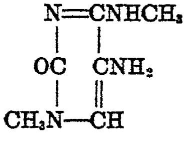
2-Oxy-4-methyl-5,6-diaminopyrimidine was prepared from 4-methyl-5-nitrocytosine (69), by suspending it in water and then reducing in the presence of aluminum amalgam under vigorous shaking, care being taken to keep the temperature below 45°C.

2-Oxy-3,4-dimethyl-5,6-diaminopyrimidine was obtained by alkylating 4-methyl-5-nitrocytosine with dimethyl sulfate and then reducing the nitro group with ferrous hydroxide (75).

Derivatives of 5-aminocytosine and 4-methyl-5-aminocytosine have been described in which the hydrogen of the amino group has been replaced by alkyl residues. In certain cases *N*-3-methyl derivatives of these substances have also been prepared.

2-Oxy-5-amino-6-methylaminopyrimidine was obtained by treating 2-ethylmercapto-6-chloropyrimidine with methylamine and then desulfurizing the product by boiling with hydrochloric acid. The resulting 2-oxy-6-methylaminopyrimidine was then nitrated by dissolving it in concentrated sulfuric acid and adding fuming nitric acid. The nitro group in the 5-position was finally reduced with ferrous hydroxide (71).

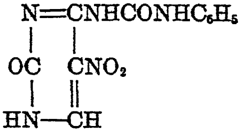
2-Oxy-3-methyl-5-amino-6-methylaminopyrimidine



was obtained by methylating the potassium salt of 5-nitromethylcytosine with methyl iodide and then reducing the resulting product (73).

2-Oxy-5-amino-6-ethylaminopyrimidine was synthesized from 2-ethylmercapto-6-chloropyrimidine by using the same procedure as has been described in the case of the corresponding methylaminopyrimidine (76).

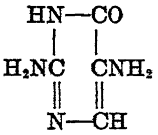
2-Oxy-5-nitro-6-phenylureapyrimidine,



has been prepared (103d) but has not been reduced to the corresponding amine.

2-Oxy-4-methyl-5-amino-6-methylaminopyrimidine was synthesized by starting with 2-ethylmercapto-4-methyl-6-chloropyrimidine and proceeding in a manner analogous to that described in the case of the corresponding 2-oxy-5-amino-6-methylaminopyrimidine (72b). *2-Oxy-4-methyl-5-amino-6-ethylaminopyrimidine* was synthesized in a similar way (74).

The only 5-amino derivative of isocytosine which has been described up to the present time is 2,5-diamino-6-oxypyrimidine.



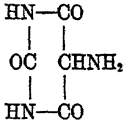
This was prepared in three different ways: (a) From isocytosine (203d) by nitrating under special conditions (100h). The structure of the resulting 5-nitro derivative was determined by converting it first into nitrouracil and then transforming the latter into the picrate of 5-aminouracil which has a definite melting point. 2,5-Diamino-6-oxypyrimidine was also readily obtained from 5-nitroisocytosine by reduction in ammoniacal solution with aluminum amalgam (100h). (b) From 5-bromoisocytosine (203f) by heating it with concentrated aqueous ammonia (100h). (c) From 2-ethylmercapto-5-amino-6-oxypyrimidine by heating it with alcoholic ammonia (100h). Of these three methods the first is the only one having practical value.

2,5-Diamino-6-oxypyrimidine is extremely soluble in water and separates from its aqueous solution with one molecule of water of crystallization. When boiled with water the solution assumes a red color and the base is apparently oxidized with the separation of a flocculent amorphous precipitate. It is a strongly diacid base and forms soluble salts with hydrochloric and nitric acids. Its sulfate and its picrate are only slightly soluble in water. It reduces the chlorides of gold and platinum to the corresponding metals and is precipitated from its aqueous solutions by phosphotungstic acid, mercuric chloride, and potassiobismuth iodide. The latter forms a brick-red precipitate. The base when heated with 20 per cent sulfuric acid at 130–140°C. in a sealed tube for three hours was partially hydrolyzed to 2-amino-5,6-dioxypyrimidine, but about 50 per cent of the original substance was recovered unchanged. The fact that this substance is relatively stable in the presence of sulfuric acid admits of the possibility of its being identical with "Kutscher's base." It is the only dioxydiaminopyrimidine which corresponds in its general properties to the base described by Kutscher as having this composition and as occurring among the hydrolytic products of yeast nucleic acid.

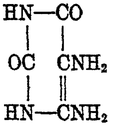
It should be noted that all 2-oxypyrimidines which contain amino groups in the 5,6-positions undergo condensation with formic acid, acetic anhydride, and urea to give purine derivatives. This type of condensation is not inhibited by the replacement of the hydrogen of the amino group nor of the hydrogen in the *N*-3-position in the ring by an alkyl hydrocarbon residue. A more detailed discussion of the various methods by which pyrimidines may be transformed into purines is reserved for later consideration.

IV. OXYAMINOPYRIMIDINES RELATED TO BARBITURIC ACID

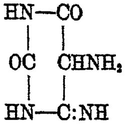
In considering this class of substances it is necessary to distinguish between (a) direct substitution products of barbituric acid which result from the replacement of hydrogen by amino or other groups, such as for example, uramil,



its homologues and other derivatives; and (b) substances like 2,6-dioxy-4,5-diaminopyrimidine (or its imido form),



or

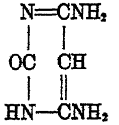


which while appearing to be substitution products of uracil actually yield barbituric acid or its derivatives on hydrolysis. It may be noted in passing that all 2,6-dioxypyrimidines which contain an amino group in the 4-position of the ring belong to the latter class. Since compounds of this type are not very numerous they will be considered first, and a discussion of uramil and products related to it will be reserved until later.

Aminoöxypyrimidines which hydrolyze to give barbituric acid or its derivatives may be separated into different subgroups arranged according to the number of oxygen atoms and amino groups present in the molecule. Any classification as arbitrary as this is open to certain objections, but these seem to be overbalanced by the advantages afforded in dealing with a somewhat confused mass of material.

Monoöxydiaminopyrimidines

The statement has already been made that oxydiaminopyrimidines are capable of existing in five different structural modifications, only two of which yield uracil on hydrolysis. Both of these have been considered in some detail. Of the remaining three isomeric possibilities only the first two have



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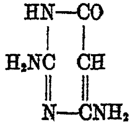
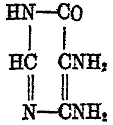


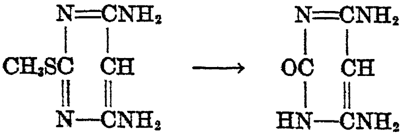
II



III

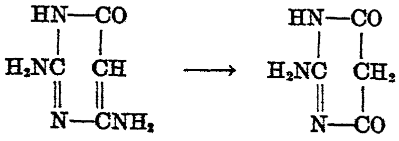
been synthesized up to the present time.

2-Oxy-4,6-diaminopyrimidine (I) was first prepared by Wheeler and Jamieson (199c) because it seemed possible that a substance having this composition might prove to be identical with a base which had been described by Kutscher (126) as resulting from the hydrolysis of yeast nucleic acid. While this did not prove to be the case, the substance which was actually obtained is nevertheless of definite theoretical importance. 2-Thio-4,6-diaminopyrimidine (188a) was made the starting point in this synthesis and was converted first into the corresponding 2-methylmercapto derivative under the action of methyl iodide. This product was then hydrolyzed by warming with hydrochloric acid:

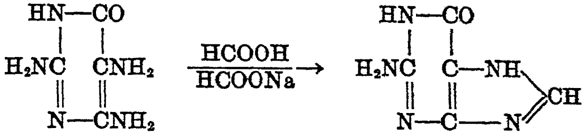


Great care must be exercised in the hydrolysis, since continued warming with hydrochloric acid results in the complete conversion of the product into barbituric acid with loss of ammonia. Under the conditions of the experiment the base separated in the form of the monohydrochloride, but when this salt is dissolved in water and ammonia added, the free base may be obtained in anhydrous condition. The latter is only slightly soluble in water and forms a characteristic picrate.

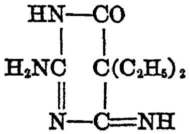
6-Oxy-2,4-diaminopyrimidine (II) was first synthesized by Traube (190d) by condensing guanidine with ethyl cyanoacetate in the presence of absolute alcohol and sodium ethoxide. This product when heated with 20–30 per cent sulfuric acid at 130–140°C. is completely decomposed, this fact eliminating at once the possibility of its being identical with "Kutscher's base." When warmed with dilute sulfuric acid, on the other hand, it hydrolyzes readily to give malonylguanidine (31b; cf. 151b, 189b).



6-Oxy-2,4-diaminopyrimidine reacts with hydrochloric and sulfuric acids to form salts. When the sulfate is dissolved in water and treated with sodium nitrite it gives a 5-nitroso derivative and this on reduction in aqueous solution with ammonium sulfide yields 2,4,5-triamino-6-oxypyrimidine. The latter, under the action of a mixture of formic acid and sodium formate, condenses to give guanine (189b).



Derivatives of 6-oxy-2,4-diaminopyrimidine have been obtained in which the hydrogen atoms in the 5-position are replaced by alkyl groups (31e), viz.,



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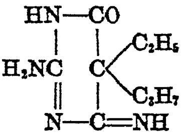
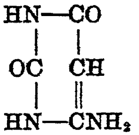


These substances are prepared by treating guanidine with the corresponding dialkylcyanoacetic esters in the presence of sodium ethoxide. Like the parent substance they hydrolyze on prolonged boiling with mineral acids, yielding the corresponding dialkylbarbituric acids.

Dioxymonoaminopyrimidines

Only two of the four structural possibilities for compounds having this composition yield barbituric acid or its derivatives on hydrolysis, viz.,



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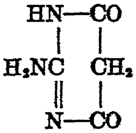
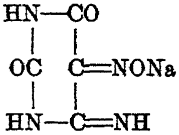


V

Both types of compounds have been synthesized and various derivatives of each prepared.

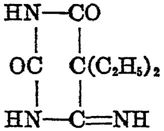
2,6-Dioxy-4-aminopyrimidine (4-aminouracil) was prepared by condensing ethyl cyanoacetate with urea in absolute alcohol solution in the presence of sodium ethoxide (31b; cf. 190a). The same substance may be obtained from cyanoacetylurea, NH_2-$CONH \cdot COCH_2CN$ (190b, 31a) by treatment with sodium hydroxide.

2,6-Dioxy-4-aminopyrimidine is both acidic and basic, dissolving in alkali and ammonia and also in concentrated mineral acids to form salts. Its sodium salt when treated with sodium nitrite in aqueous solutions yields a salt of the corresponding violuric acid:



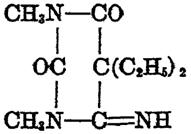
N-Alkyl derivatives of 2,6-dioxy-4-aminopyrimidine may be obtained by condensing alkyl ureas with ethyl cyanoacetate in the presence of sodium ethoxide,—*N*-3-methyl-4-amino-2,6-dioxypyrimidine being obtained from methylurea (190b, 31c, 97b) and an *N*-1-*N*-3-dimethyl derivative from dimethylurea (190i; cf. 156). Both have been transformed into the corresponding 5-nitroso and 5-amino compounds by application of the same general procedure as has already been described in the case of 2,6-dioxy-4-aminopyrimidine. The resulting methylated 4,5-diaminopyrimidines yield 3-methylxanthine (190h; cf. 43) and 1,3-dimethylxanthine, respectively, under the action of a mixture of formic acid and sodium formate. 1,3,7-Trimethylxanthine and 1,3-dimethyluric acid may also be obtained from 1,3-dimethyl-2,6-dioxy-4,5-diaminopyrimidine on treatment with methyl formate and with ethyl chloroformate and ammonia (190h), respectively.

Derivatives of the tautomeric modification of 2,6-dioxy-4-aminopyrimidine in which two hydrogens in the 5-position have been replaced by alkyl groups have also been prepared. For example, *C*-diethyl-4-iminobarbituric acid,



is obtained by condensing ethyl diethylcyanoacetate with urea in the presence of sodium ethoxide. Other representatives which have been prepared by substituting the corresponding alkyl cyanoacetic esters for ethyl cyanoacetate in this type of reaction are, for example, *C*-propyl, *C*-ethylpropyl, *C*-dipropyl-, and *C*-dibenzyl-4-aminobarbituric acids. These substances all hydrolyze on prolonged boiling with mineral acids to give the corresponding alkylated barbituric acids (31d).

Alkyl derivatives combining both of the two preceding types have also been reported. For example, 5-diethyl-4-iminobarbituric acid reacts with methyl iodide in the presence of sodium methoxide to give the corresponding *N*-1-methyl-, *N*-3-methyl-, and *N*-1-*N*-3-dimethyl derivatives (31d). *N*-1-Methyl-5-diethyl -4-iminobarbituric acid also reacts with methyl iodide in the presence of sodium methoxide to give a dimethyl derivative which is not identical with the *N*-1-*N*-3-diethyl-4-iminobarbituric acid referred to above. It is an interesting fact that these two isomeric products



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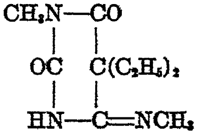
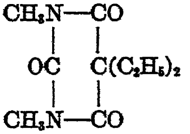
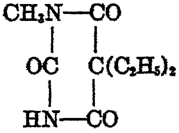


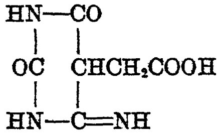
hydrolyze under the prolonged action of mineral acids to give diethylmalonyldimethylurea and diethylmalonylmethylurea respectively.



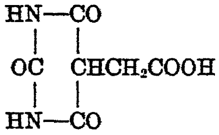


In this connection it may be noted that *N*-alkyl derivatives of the above types hydrolyze to give open chain compounds and in this respect differ from the preceding class of substances which contain hydrogen atoms in both the *N*-1 and *N*-3 positions and which hydrolyze under the same conditions to yield ring compounds (alkylbarbituric acids).

4-Iminobarbituryl-5-acetic acid has been prepared by a modification of the general method of procedure which has just been discussed, and may be obtained by digesting ethyl cyanosuccinate with urea. During the process the ester group was saponified and the imino group was also hydrolyzed to some extent. This was shown by the fact that while a brown precipitate consisting of



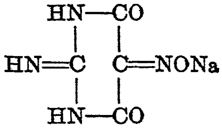
was obtained as the immediate product of the reaction, the filtrate from this when concentrated deposited crystals of barbituryl-5-acetic acid (105).



4,6-Dioxy-2-aminopyrimidine (V), malonylguanidine, was first synthesized by Michael (150, 151a, 149) as a result of condensing guanidine rhodanide with the sodium salt of diethyl malonate in absolute alcohol. It has also been prepared by adding two molecular quantities of free guanidine to one molecular quantity of diethyl malonate in the absence of any solvent. The product in this case forms a solid crystalline mass, which consists of the guanidine salt of malonylguanidine. This dissolves readily in water to give a strongly alkaline solution from which, on the addition of dilute acetic acid, free malonylguanidine is precipitated as a crystalline solid (189a).

Malonylguanidine when suspended in water and treated with bromine gives a dibromo derivative having the composition $C_4H_3O_2N_3Br_2$ (189a). Treated with fuming nitric acid, it yields a

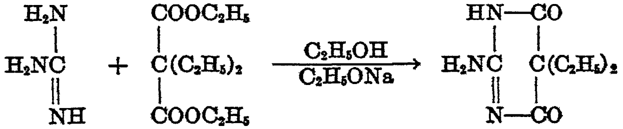
5-nitro derivative and with sodium nitrite, the sodium salt of the corresponding isonitroso derivative, viz.,



2-Iminovioluric acid
(sodium salt)

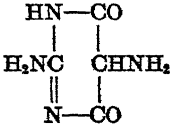
The corresponding ammonium salt of 2-iminovioluric acid may be obtained by dissolving malonylguanidine in aqueous ammonia and adding an equivalent amount of sodium or potassium nitrite. Dilute hydrochloric acid is then gradually added until the solution is strongly acid, when it is diluted and treated with an excess of ammonia. If sufficiently dilute the clear solution develops a dark violet coloration on boiling and when cooled deposits violet colored needles which consist of the ammonium salt of 5-isonitrosomalonylguanidine. This salt may be used in the preparation of the corresponding 2,5-diamino derivative of 4,6-dioxypyrimidine.

C-Dialkyl malonylguanidines have been prepared by condensing alkylmalonic esters with guanidine in absolute alcohol under the action of sodium ethoxide as the condensing agent (45a). This reaction is of general application.

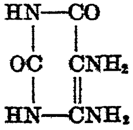


Dioxydiaminopyrimidines

Pyrimidines which contain two oxygen atoms and two amino groups and which on hydrolysis yield barbituric acid or its derivatives may exist in two different structural modifications (VI and VII):



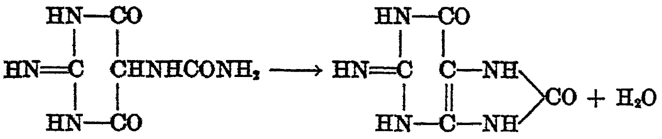
VI



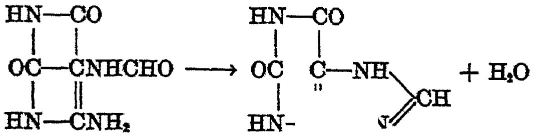
VII

Both types of substances have been synthesized but very little is known regarding their derivatives. *4,6-Dioxy-2,5-diaminopyrimidine* (VI) was prepared by Traube (189c) by dissolving the ammonium salt of 5-isonitrosomalonylguanidine in dilute hydrochloric acid and saturating the solution with hydrogen sulfide. It is interesting to note that reductions of this type with hydrogen sulfide in acid solution are very unusual, since the observation has frequently been made that nitro and nitroso groups are unacted upon by this gas except in the presence of alkali (113a; cf. 4c).

4,6-Dioxy-2,5-diaminopyrimidine dissolves in boiling aqueous potassium cyanate, and this solution when cooled and treated with hydrochloric acid yields the corresponding urea (189d, 38d). According to Fischer the latter may be condensed to the corresponding purine if it is warmed with 20 per cent hydrochloric acid.



2,6-Dioxy-4,5-diaminopyrimidine (VII) has also been prepared by Traube (190f). Like its isomer it was obtained from the corresponding 5-isonitroso derivative under the reducing action of hydrogen sulfide. The product behaves like all pyrimidines which contain amino groups in the 4,5-positions and is readily transformed into the corresponding purine under the action of formic acid and sodium formate. It is interesting to note that in this case, however, the reaction takes place in two stages,—the primary product of the reaction consisting of a formyl derivative which must be isolated and heated at 220°C. in order to effect a closure of the imidazole ring (190g):



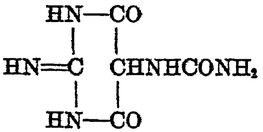
2,6-Dioxy-4,5-aminopyrimidine also condenses readily with urea to give quantitative yields of uric acid (101c).

The syntheses of 4,6-dioxy-2,5-diaminopyrimidine and 2,6-dioxy-4,5-diaminopyrimidine have played a very important rôle in solving what was for many years a most perplexing problem in the field of biochemistry, since without a knowledge of the configuration of these two substances the structure of divicine and vicine could not have been elucidated. As is generally known, divicine, vicine, and convicine have been frequently reported as resulting from the hydrolysis of various plant tissues. All three were isolated from vetch seeds and also from beans by Ritthausen and his coworkers (170, 168, 169, 171, 167). Vicine has also been isolated from beet juice by Lippmann (145), from vetch seeds and peas by Schulze (176), and also from vetch by Winterstein (210). Both vicine and convicine are well-crystallized substances slightly soluble in water, vicine being distinguished from convicine by the fact that it forms a soluble sulfate. Both are nucleosides since they have been found to yield a sugar and a base on hydrolysis. In the case of vicine the base is divicine (168), and the sugar is dextrose (40, 128, 143).

The elucidation of the structure of divicine was accomplished in the following stages. Schulze and Trier (177a) were the first to suggest that a structural relationship might exist between it and pyrimidines. This idea was developed in greater detail by Johnson (80) and by Johnson and Johns (101a) who called attention to the similarity in composition between divicine and the isomeric dioxydiaminopyrimidines described by Traube. Both of these substances had been isolated by Traube in the form of their sulfates. The latter were again prepared by Johnson and Johns according to Traube's method and the free bases separated by treatment with the exact amount of sodium hydroxide. In comparing these two free bases with divicine a series of precipitation and color tests were applied which directly paralleled similar tests described by Ritthausen (169). The results as tabulated (101b) indicated so close an agreement in chemical behavior between 2,6-dioxy-4,5-diaminopyrimidine and divicine as to lead to the conclusion that the two substances were identical.

The further discovery that 2,6-dioxy-4,5-diaminopyrimidine condenses readily with urea to give uric acid while 4,6-dioxy-2,5-diaminopyrimidine does not, led to the statement that conclusive evidence in support of the former configuration might be obtained by fusing divicine with urea. In applying this reaction to natural divicine, Fischer (40) obtained negative results, but the data furnished by this experiment was of such a character as not to disprove completely the configuration for divicine suggested by Johnson and Johns. In fact, Fischer was led to conclude that divicine and 2,6-dioxy-4,5-diaminopyrimidine were stereoisomers, the latter representing a maleinoic modification.

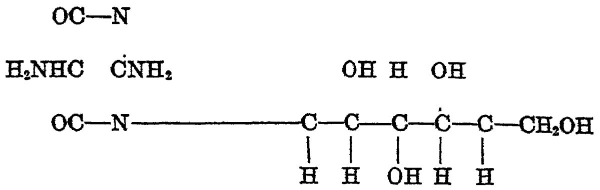
This conclusion was not accepted by Levene who, on the other hand, as a result of independent investigations during the same year was able to call attention to the fact that the properties of divicine coincide very closely with those of *4,6-dioxy-2,5-diaminopyrimidine.* Both form anhydrous sulfates, both give off 50 per cent of their nitrogen as nitrogen gas when treated with nitrous acid, and neither condenses with urea to give uric acid (128). This configuration for divicine was finally established by Levene as a result of further investigations undertaken in coöperation with Senior (143) by means of which he was able to demonstrate that divicine yields (a) guanidine with a cleavage of the pyrimidine ring under the oxidizing action of potassium chlorate and hydrochloric acid, and (b) 2-iminopseudouric acid,



$$\begin{array}{ccc} & \mathrm{HN{-}} & \mathrm{CO} \\ & | & | \\ \mathrm{HN{=}} & \mathrm{C} & \mathrm{CHNHCONH_2} \\ & | & | \\ & \mathrm{HN{-}} & \mathrm{CO} \end{array}$$

on treatment with potassium cyanate and hydrochloric acid.

The following configuration for vicine was developed by Levene on the basis of this evidence taken in conjunction with the fact (a) that both vicine and divicine yield 50 per cent of their nitrogen in the form of nitrogen gas when treated with nitrous acid, thus pointing conclusively to the presence of two free primary amino groups in each of these substances, and (b) that vicine had been shown to give divicine and dextrose on hydrolysis (143):



The ease with which vicine is hydrolyzed is, moreover, in accord with the assumption that a dihydropyrimidine nucleus, as represented above, is present in its molecule. Nucleosides which contain cytosine and other unsaturated pyrimidine ring structures are characterized by their relatively great resistance to the action of hydrolyzing agents.

The configuration of *convicine,* which occurs along with vicine in vetch and broad beans, has not as yet been conclusively established. Ritthausen concluded that convicine, like vicine, was glucosidic in character. When hydrolyzed with 20 per cent sulfuric acid, it yields alloxantin in amounts corresponding to 36 to 37 per cent of its weight (169). Prior to this time Schulze and Trier (177b) had suggested the following equation to account for the hydrolysis of convicine,

$$C_{20}H_{18}N_6O_{16}\cdot 2H_2O + 4H_2O \rightarrow C_8H_6O_4N_8\cdot 2H_2O + 2NH_3 + 2C_6H_{12}O_6$$

and at the same time advanced the hypothesis that convicine might be related structurally to the pyrimidine nucleosides.

In speculating upon these relationships, Johnson in 1914 pointed out that convicine agrees exactly in composition with either an aminoglucoside of dialuric acid or a glucoside of uramil. At the present time this hypothesis as to the possible configuration of convicine has been somewhat modified as a result of investigations carried on by T. B. Johnson in collaboration with H. J. Fisher (93). In preparing convicine from broad beans by a modification of the methods described by Ritthausen and Levene in isolating vicine, Johnson and Fisher obtained a product which corresponded to the later formula, $C_{10}H_{15}O_3H_8\cdot H_2O$, proposed by Ritthausen. Hydrolysis of this substance yielded alloxantin in crystalline form and glucose, which was obtained from the filtrate in the form of glucosazone. Since no glucosamine hydrochloride could be detected when hydrochloric acid was used for the hydrolysis, there is no evidence for the assumption that glucosamine is linked to the base in convicine.

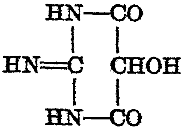
Supposing that $C_{10}H_{15}O_3H_8 \cdot H_2O$ correctly represents the composition of convicine it is obvious that alloxantin itself cannot be present in the molecule in the form of a glucoside. A base of the composition $C_4H_5N_3O_3$ which might be expected to result after the splitting-off of the sugar must be of such a configuration that (a) it will lose ammonia readily during the process of hydrolysis and (b) it will possess some well-defined relationship to alloxantin.

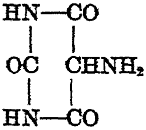
In considering this second prerequisite it may be said that while the actual molecular configuration of alloxantin has not as yet been conclusively determined, it has nevertheless been definitely demonstrated that an equilibrium is established between alloxan, dialuric acid, and alloxantin when any one of these substances is dissolved in water (18, 19, 20).

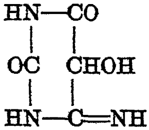
$$\text{Alloxan} + \text{dialuric acid} \rightleftarrows \text{alloxantin}$$

It follows therefore that if either alloxan or dialuric acid were formed as a result of the hydrolysis of convicine, the presence of alloxantin among the hydrolytic products could be readily accounted for, since it is much less soluble than either of the other two substances and would, therefore, tend to separate in the form of a precipitate.

In brief, a base of the composition $C_4H_5N_3O_3$ and of such configuration as to lose ammonia readily to give either alloxan or dialuric acid, would satisfy the structural requirements demanded by convicine. Since it is obvious that an amino derivative of alloxan would contain too many atoms to meet these conditions, the problem is limited to a consideration of the imino derivatives of dialuric acid. Three structural isomers are possible, namely, 2-iminodialuric acid (VIII), uramil (IX), and 4-iminodialuric acid (X):


VIII


IX


X

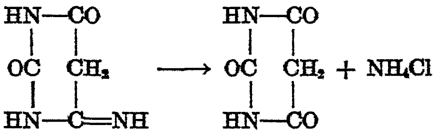
These three substances may now be considered separately in a further development of this analysis of the problem.[11]

2-Iminodialuric acid (VIII) would be expected to give guanidine in any cleavage of the pyrimidine molecule resulting from the oxidizing action of potassium chlorate and hydrochloric acid.[12] Actually convicine has been observed to yield urea (which was isolated as the xanthyl derivative) when oxidized under these conditions. Moreover there is no instance recorded in the literature where an imino group in the 2-position in a uracil or barbituric acid derivative is hydrolyzed under the action of dilute acids with the evolution of ammonia.[13]

Uramil (IX) would be expected to give the corresponding pseudouric acid under the action of potassium cyanate,[14] while actually convicine is recovered unchanged when treated with this reagent. Moreover there is again no instance recorded in the literature of an amino group in the 5-position being easily split off from a pyrimidine by hydrolysis.

4-Iminodialuric acid (X), on the other hand, which has recently been synthesized by Bogert and Davidson (isouramil (21)), appears to fulfill all requirements. It is known, for example, that pyrimidines which contain an imino group in the 4-position hydrolyze readily under the action of dilute mineral acids with the evolution of ammonia. In the case of the above substance this hydrolysis actually results in the formation of dialuric acid.

Two examples of this type of hydrolysis may be cited, out of the many to be found in the literature, as pertinent to the present discussion. 4-Aminouracil, which represents a reduced form of 4-iminodialuric acid, is transformed into barbituric acid and ammonia when treated with dilute hydrochloric acid:



$$\begin{array}{lcl} \mathrm{HN{-}CO} & & \mathrm{HN{-}CO} \\ \;|\quad\;\;| & & \;|\quad\;\;| \\ \mathrm{OC\quad CH_2} & \longrightarrow & \mathrm{OC\quad CH_2} + \mathrm{NH_4Cl} \\ \;|\quad\;\;| & & \;|\quad\;\;| \\ \mathrm{HN{-}C{=}NH} & & \mathrm{HN{-}CO} \end{array}$$

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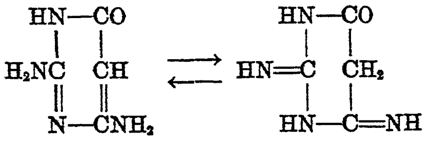
[11] Only the lactam CO.NH constructions are considered in this review.

[12] Compare the formation of guanidine from divicine (143).

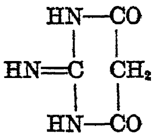
[13] When the imino group occupies the 2-position in certain tetrahydropyrimidines it is easily hydrolyzed with evolution of ammonia (unpublished results).

[14] Compare the formation of 2-iminopseudouric acid from divicine (143).

2,4-Diamino-6-oxypyrimidine, which can also be expressed as a diimino derivative of barbituric acid,

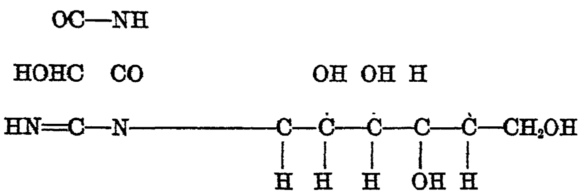


reacts in a similar way to give malonylguanidine,



and ammonia when warmed with dilute mineral acids. This second illustration is particularly significant because it serves to emphasize the difference in the stability of amino and imino groups in the 2- and 4-positions respectively.

It has been observed moreover that convicine contains one free amino group, since it yields a quantity of free nitrogen gas equivalent to such a configuration when treated with nitrous acid. From this it would seem to follow that the sugar linkage cannot be located on this group. All of the above relationships may therefore be embodied in the following tentative formula for convicine:



This formula also accounts for the relative ease with which convicine undergoes hydrolysis.[15]

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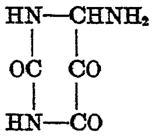
[15] Compare the similar behavior of vicine, which is also accounted for by the presence of a dihydropyrimidine nucleus in the glucosidic combination, the latter having been observed to split as readily as in the case of the common glucosides.

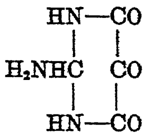
V. DERIVATIVES OF BARBITURIC ACID AND THEIR RELATION TO MEMBERS OF THE PURINE GROUP

Several different molecular configurations are theoretically possible in which three oxygen atoms and one amino group are associated in a reduced pyrimidine ring structure such as, for example, pyrimidines I and II,



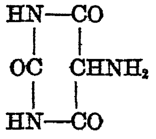
I

and

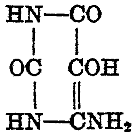


II

but no compound corresponding to either of these two formulas has as yet been described in the literature. The only pyrimidines possessing this general composition which have been studied are 5-aminobarbituric acid or, as it is more commonly known, uramil (III), and its isomer, isouramil (IV), recently synthesized by Bogert and Davidson (21).

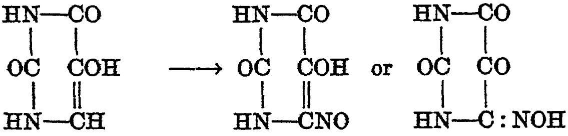


III



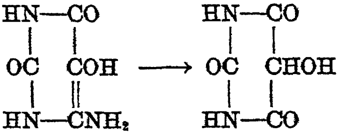
IV

Isobarbituric acid (I) served as the starting point for the synthesis of isouramil. Davidson and Bogert have observed that this pyrimidine interacts with nitrous acid to give a nitroso compound which may be expressed by either of the two formulas, VI or VII. On reduction of this nitroso derivative with ammonium sulfide, the nitroso group is easily reduced and the pyrimidine is converted into isouramil (IV), whose structure is established by the fact that it undergoes hydrolysis in acid solution with evolution of ammonia and formation of dialuric acid (VIII). Isouramil does not melt below 290°C., and is insoluble in hot water, alcohol, or acetic acid. It dissolves immediately in sodium hydroxide solution, ammonia, and dilute hydrochloric acid, and by the oxidation of nitric acid it is oxidized to alloxan.



Isobarbituric acid

V VI VII

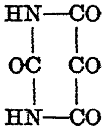


Isouramil Dialuric acid

IV VIII

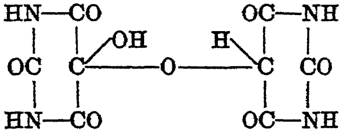
The extremely interesting and important pyrimidine uramil (III) has held the attention of research workers from very early times and has been intimately associated with developments in the fields of both pyrimidine and purine chemistry. Uramil was first described by Liebig and Wöhler in connection with their investigations on uric acid, which have since become classic. Their discovery may be said to mark the beginning of a century of research during which time both pyrimidines and purines have been intensively studied. The result of this work was to establish the molecular configurations of the more important substances belonging to each of these two classes and in this way to elucidate the interrelationships existing not only between individuals of the same class, but also between the two general groups of compounds. In the field of purine chemistry these developments culminated in the classic investigations of Emil Fischer and his coworkers, which will be referred to again later. The fact that in the early stages of their development the chemistry of pyrimidines was so closely interwoven with that of purines makes it difficult to discuss one without reference to the other. This is particularly true in the case of uramil, so that a brief preliminary survey of the early investigations in the field of uric acid seems necessary to any clear understanding of the chemistry of uramil and its derivatives.

Uric acid was discovered by Scheele in 1776. Forty years later Brugnatelli (25, 26) oxidized it with nitric acid and chlorine water and isolated the pyrimidine *alloxan.*



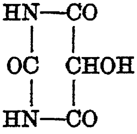
In the following year the English chemist, Prout (166), repeated the work of Scheele and found that the product which was obtained by oxidizing uric acid with nitric acid reacted with ammonia to form an intense red color which was destroyed by acids. This led to the discovery of *murexide,* which has since been found to represent the ammonium salt of purpuric acid and which finds application at the present time as a color test for uric acid and related purines. In continuing this investigation Prout (165) was able to show that alloxan may also be obtained from murexide on oxidation.

It was not until more than half a century after the discovery of uric acid by Scheele that a systematic study of its properties was undertaken by Wöhler and Liebig (211a). It was then prepared in pure condition, analyzed, and its transformations under the action of different oxidizing agents, at different conditions of temperature and concentration, investigated. The results obtained from these experiments demonstrated that the process of oxidation involved the formation of a number of substances in addition to those already described. It was found, for example, that while uric acid reacts with concentrated nitric acid to give alloxan, it also reacts with dilute nitric acid to give *alloxantin.* These investigations led moreover to the discovery of a definite relationship between alloxantin and alloxan, since they may be transformed one into the other under the action of oxidizing and reducing agents respectively. Further investigations of alloxan (which was obtained in pure condition and correctly analyzed) revealed the fact that under the action of reducing agents it yielded not only alloxantin but also the pyrimidine *dialuric acid,*



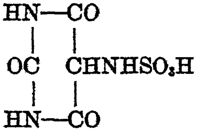
Alloxantin

and



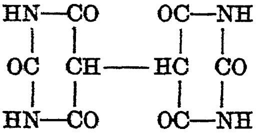
Dialuric acid

and under the action of sulfuric acid, another new and equally important pyrimidine, namely, *thionuric acid:*



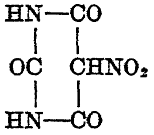
The isolation of the latter led directly to the discovery of *uramil,* which is readily formed from thionuric acid under the hydrolyzing action of dilute mineral acids. The structure of these substances as represented above was not of course established until a number of years later, because the theory of organic chemistry had not at that time progressed far enough to admit of such an interpretation of the molecular formulas which were obtained as a result of these experiments.

The investigations of Liebig and Wöhler were continued by two of their pupils, Schlieper and Gregory, who published important papers on alloxan, hydurilic acid, nitrohydurilic acid, allituric acid, and dilituric acid. It should be noted in this connection that Schlieper (174), in the course of preparing alloxan, incidentally succeeded in isolating *hydurilic acid.*



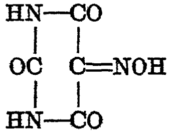
This discovery was important because of the fact that this substance was made the starting point for later investigations by

Baeyer. Schlieper also obtained *dilituric acid* (nitrobarbituric acid),

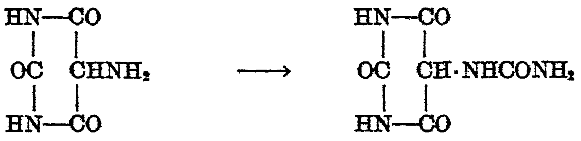


as one of the products formed in the oxidation of alloxantin by nitric acid.

Renewed impetus to the further study of the interesting relationships existing between pyrimidines and purines was supplied by Baeyer, a pupil of Schlieper, who in 1863 was able to apply the theories of structural organic chemistry, as they had by that time been developed by Kekulé, to a systematic elucidation of the molecular configurations of these various compounds. As has been said, the starting point of Baeyer's investigations was hydurilic acid. This he succeeded in transforming into violuric acid,



as a result of oxidation with nitric acid, demonstrating at the same time that violuric acid readily yields dilituric acid on further oxidation with the same reagent. From the evidence furnished by these and other experiments he was led to the important conception that a direct transition from barbituric to uric acid might be established through the intermediate formation of bromobarbituric acid, dibromobarbituric acid, dialuric acid, alloxan, violuric acid, dilituric acid, uramil, and pseudouric acid (5). The latter substance was obtained from uramil under the action of aqueous potassium cyanate (4a),



but its conversion into uric acid was not accomplished until many years later, when Fischer and Ach (42a) finally succeeded in condensing the urea side chain to an imidazole ring with the elimination of one molecule of water under the action of molten oxalic acid.

The period of activity initiated by Baeyer was also characterized by the following achievements: A correct structural formula was assigned to barbituric acid by Mülder (155) and its synthesis from urea and malonic acid under the action of phosphorus oxychloride was accomplished by Grimaux (61). The synthesis of nitroso-, nitro-, and amino-malonic acids was effected and attention directed to the relationship of these substances to the corresponding derivatives of barbituric acid (5). The conclusion of this period of great productivity was finally marked by the brilliant speculations of Medicus (147), who proposed structural formulas for uric acid, guanine, and other purines, which were not only illuminating at the time, but which have since been demonstrated to be correct.

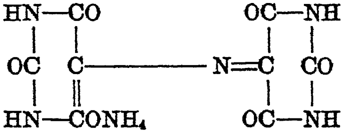
In summary, it may again be said that this general historical review has been introduced at this point in order to call attention to the fact that uramil is related on the one hand to such complex combinations as uric acid, murexide, purpuric acid and alloxantin, and on the other hand, to the relatively simpler derivatives of barbituric acid. Because of this definitely established connection it seems desirable in considering the various methods by which uramil may be prepared, to arrange them in three groups representing:

I. The hydrolysis of complex structures, the exact configuration of which in certain instances has not yet been conclusively determined, as, for example, murexide.
II. Transitions (a) from barbituric acid and (b) from alloxan.
III. Direct synthesis from simpler units.

It is hoped that such an arrangement may serve not only to simplify a discussion of the methods for preparing uramil, but also aid in the subsequent treatment of its various alkylated derivatives.

I. In considering methods of preparation belonging to the first group, nothing further need be said in regard to the oxidation and hydrolysis of uric acid. This process is one which while very complex, nevertheless involves the formation of murexide, or other salts of purpuric acid, and alloxantin as primary products. These may therefore be considered respectively as starting points in the preparation of uramil.

Murexide, as has already been said, is now regarded as the ammonium salt of purpuric acid. The latter is not itself capable of existing in the free state, although many of its derivatives are known. The formula for murexide which is most generally accepted as correct is one proposed by Möhlau (153, 154; cf. 160a, 180a), viz.,

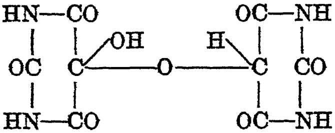


Purpuric acid, from which this salt is derived, might therefore be assumed to represent a condensation product of uramil with alloxan. It might be assumed further that the resolution of this complex on hydrolysis would serve to define this relation, but unfortunately the experimental evidence is confusing. For example, murexide has been observed under certain conditions to give uramil (46 per cent), alloxan (47 per cent), and ammonia (154), while under still other conditions it breaks down to give an ammonium salt of dialuric acid and alloxan. In the latter case uramil could not be assumed to represent a primary product from which murexide forms or into which it hydrolyzes (160a). In general it may be said that the character as well as the quantity of the decomposition products that have been obtained from murexide and also from potassium purpurate depend upon conditions of temperature and concentration even under the action of the same hydrolytic agent (160b). Murexide has been synthesized by condensing molecular quantities of uramil and alloxan in the presence of ammonium carbonate (154).

$$\underset{\text{Uramil}}{C_4H_5O_3N_3} + \underset{\text{Alloxan}}{C_4H_2O_4N_2} + (NH_4)_2CO_3 \rightarrow \underset{\text{Murexide}}{2C_8H_8O_6N_6} + 2H_2O + 2CO_2$$

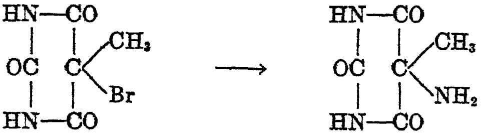
It has also been prepared from the ammonium salt of dialuric acid and alloxan under the action of ammonium acetate and ammonium carbonate (160b).

Alloxantin has been found to occur among the oxidation products of uric acid, the hydrolytic products of murexide, and the reduction products of alloxan. It has also been prepared by condensing alloxan with dialuric acid and is generally thought to possess the following structure:

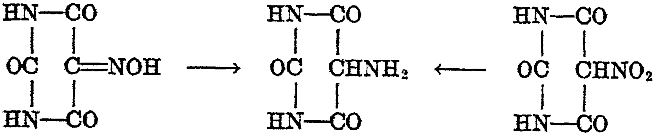


Treated with ammonia and amines it reacts to give uramil or alkylated derivatives of uramil, respectively (154, 160b, 180a). The salts of purpuric acid with ethylamine and methylamine have also been observed to yield 7-methyl- and 7-ethyl-uramil, respectively (154).

II (a) In preparing uramil from barbituric acid a number of different methods of procedure are possible. For example, 5-bromobarbituric acid when treated with ammonia yields uramil; the corresponding 5-alkyl-5-bromobarbituric acids behave similarly (45c).

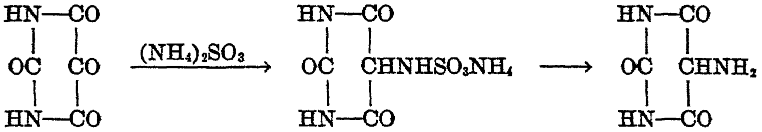


Uramil may also be prepared from violuric and dilituric acids on reduction. *N*-1- and *N*-3-alkyluramils can be prepared from the corresponding compounds in the same way (4b, 179, 208, 186).



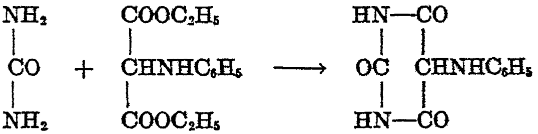
It may be obtained from thionuric acid (211a) and also from the ammonium salt of dialuric acid (160a) on hydrolysis.

(b) Uramil and its monoalkyl derivatives may be prepared by starting with alloxan. In this case also it is possible to proceed in a number of different ways. Alloxan may be treated with ammonium sulfite or with the sulfites of primary amines, respectively. This method is capable of very wide application but cannot be used successfully with the sulfites of secondary amines (160d). The mechanism of the reaction is thought to consist in the formation of a salt of thionuric acid as a primary product and its subsequent hydrolysis in the presence of acids (211b, 186, 44, 38b).



Alloxan or its alkyl derivatives may be treated with hydroxylamine. This results in the formation of the corresponding oxime (violuric acid), which may then be reduced as described under II (a). Uramil may also be prepared by treating alloxan with phenylhydrazine and then reducing the hydrazone with tin and hydrochloric acid (125). The same hydrazone may also be obtained by starting with barbituric acid on treatment with diazobenzene hydrochloride. It will be noted in general that all of the above methods for preparing uramil from alloxan almost exactly parallel methods which have been described under II (a).

III. Finally 7-phenyluramil, for example, may be directly synthesized by condensing urea with diethyl anilinomalonate in the presence of sodium ethoxide (114c):



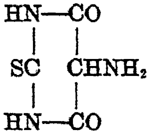
This method finds somewhat more general application in the synthesis of thiouramils by means of condensations with thiourea and will be referred to again later.

Uramil is almost completely soluble in hot water, from which it crystallizes on cooling in colorless needles which redden on exposure to the air. It reacts with alkalis to form salts but on prolonged boiling is resolved into urea and the salts of aminomalonic acid. Boiled with ammonia it is transformed into murexide and with nitric acid into alloxan. When dissolved in aqueous potassium cyanate it yields pseudouric acid and the latter, when heated with molten oxalic acid or when digested with hydrochloric acid, undergoes condensation to form uric acid (42a, 38c). Treated with ethyl cyanate or phenyl cyanate respectively, uramil is transformed into the corresponding substituted pseudouric acids, which may then be condensed to yield derivatives of uric acid which contain hydrocarbon residues in the 9-position (2, 39). As has been stated, a variety of different products may be obtained by condensing uramil with alloxan or with dialuric acid under different conditions (154, 160d). When treated with acetic anhydride and sodium acetate, uramil reacts to give a 7-acetyl derivative. The same product is formed under the action of acetyl chloride (160c).

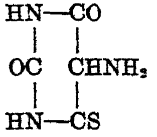
Alkylated derivatives of uramil may be obtained under a variety of different conditions. The preparation of substances belonging to this class has already been referred to in connection with the different methods for preparing uramil. In summary, it may be said that *N*-1 and *N*-3 derivatives are commonly obtained by starting with the corresponding mono- or di-substituted barbituric acids or alloxans respectively and proceeding as described under II (a) and (b). They may also be prepared from alkylated alloxantins by treatment with ammonia and from alkylated derivatives of purpuric acid on hydrolysis (154, 160d). 7-Alkylated uramils may be obtained (1) by treating alloxan, or its *N*-1-*N*-3 derivatives, respectively, with alkyl sulfites and then hydrolyzing the product; (2) by treating alloxantin or purpuric acid with alkyl amines; (3) by synthesis from urea and amino compounds corresponding to diethyl anilinomalonate. All of the substances obtained in these various ways react with aqueous potassium cyanate to give the corresponding pseudouric acids, which in most cases condense to form alkylated uric acids containing substituting groups in the 1-, 3-, and 7-positions, respectively or collectively. In general it is possible to distinguish pseudouric acids from the corresponding uric acids by the fact that the latter yield alloxantins while the former do not (38a; cf. 42b). In the case of pseudouric acids which have been obtained by treating uramil with alkyl cyanates the resulting uric acids contain substituents in the 9-position.

C-5-Alkyl derivatives of uramil may be prepared from 5-bromo-5-alkylbarbituric acids on treatment with ammonia (45b). Substances belonging to this class react with potassium cyanate to give pseudouric acids, but the latter do not undergo condensation with the formation of imidazole rings.

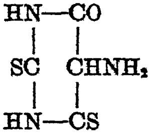
Since the term "uramil" is commonly used to include thiouramils, these must now be considered briefly. Two isomeric configurations are possible for monothiouramils, viz.,

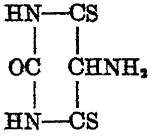


and



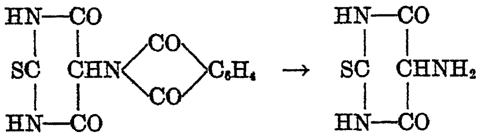
and also two for uramils in which two oxygen atoms have been replaced by sulfur (114a).





Both types of monothiouramils are known.

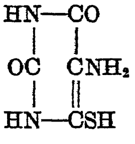
2-Thiouramil may be prepared by condensing thiourea with the hydrochloride of diethyl aminomalonate in the presence of sodium ethoxide. Under these conditions the product separates in the form of a sodium salt. The latter, when dissolved in water and treated with acetic acid, yields the free base (113b). The same substance may be obtained by condensing thiourea with phthalimidomalonic ester and then hydrolyzing the resulting product (114a).



In the latter case, however, the yield is not as good as in the first case. 2-Thiouramil is not desulfurized by warming with mineral acids and when warmed with sodium hydroxide it decomposes to give the sodium salt of aminomalonic acid. When dissolved in aqueous potassium cyanate it reacts to give 2-thiopseudouric acid (113b). Substituted 2-thiouramils have been obtained by condensing thiourea and allylthiourea, respectively, with diethyl anilinomalonate (114a).

2-Thiovioluric acid may be prepared by condensing thiourea with diethyl nitrosomalonate (113b). The corresponding 2-methylmercaptovioluric acid has also been synthesized (199d). This on reduction gives 2-methylmercaptouramil.

4-Thiouramil has been synthesized by Traube (188a) and has also been prepared by reducing potassium urate with ammonium sulfide at 155–160°C. (41a; cf. 157, 192). The product reacts with potassium cyanate to give the corresponding pseudouric acid. The latter cannot be condensed to form the corresponding uric acid (41b). 4-Thiouramil is a very strong monobasic acid. This is assumed to be due to the fact that in its tautomeric form



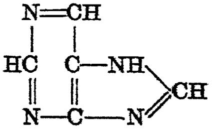
it contains a hydrogen atom in union with sulfur. The replacement of this hydrogen by metals results in the formation of salts which are very stable and which are not hydrolyzed under the action of acetic acid. 1,3-Dimethyl-4-thiouramil has also been prepared both by Fischer and Ach and by Traube (188a).

In general it may be said that monothiouramils are substances which have physiological interest but which do not react readily to give the corresponding pseudouric acids. No attempts to synthesize dithiouramils have been reported in the literature.

In connection with the use of thioureas and pseudothioureas in the synthesis of pyrimidines it may be noted that both types of substances have been employed extensively for condensation reactions leading to the formation of this cycle. When the condensation product consists of a 2-thiopyrimidine, it can frequently be transformed into the corresponding 2-oxypyrimidine under the action of chloroacetic acid, or into the corresponding 2-methylmercapto derivative under the action of methyl iodide in the presence of sodium methoxide. Substances belonging to the latter class usually hydrolyze readily to the corresponding 2-oxypyrimidines when warmed with mineral acids. The application of these two methods of synthesis has represented one of the most important contributions to pyrimidine chemistry during the present century, and has been particularly valuable in preparing pyrimidines of known structure, since the presence of a sulfur atom or a mercapto group in the 2-position can be utilized to limit the substitution of various other groups to the 2-position of the ring. It should be noted, however, that the presence of certain substituents in the ring tends to interfere with both of the above methods for the ultimate desulfurization of the products which may be prepared in this way. Notable illustrations of this have been observed in cases where position 5 is occupied by amino or substituted amino groups (89b, 78b, 114b), and also in cases where position 6 is similarly occupied (108b). It has been observed, however, that the influence of nitrogen in these same positions in the purine molecule is not so potent. Thus for example, 2-thio-4,5,6-triaminopyrimidine is not desulfurized under the action of acids like formic acid but undergoes condensation to give 2-thioadenine, the latter then being readily desulfurized to form adenine (188b). Other illustrations showing the ease with which 2-thiopurines may be hydrolyzed are recorded in the literature.

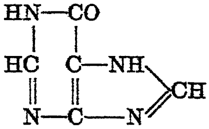
Since the chemistry of the uramils is so closely associated with the chemistry of the purines, it seems desirable at this point to refer briefly to some of the later developments in both fields. It was pointed out at the beginning of this chapter that certain phases in the early development of pyrimidine chemistry could be attributed to the fact that uramil and related compounds had been observed to result from the oxidation and hydrolysis of uric acid. Since then other purines which occur more or less abundantly in nature (notably caffeine, theobromine, guanine, and adenine) have also been found to yield pyrimidines when treated in the same or a similar manner. In attempting to explain the relationship between these two classes of compounds the problem has been attacked in two ways, i.e, by studying the transformations and cleavage products of the purines and by synthesizing them from pyrimidines.

As a result of research in the field of purine chemistry, many new substances have been discovered, the configurations of their molecules have been correlated, transformations of one into the other have been effected, and finally they have in many instances been resolved into the corresponding pyrimidines. The achievements of Emil Fischer and his coworkers have been especially conspicuous in developments of this kind. Since this work has been very thoroughly reviewed and summarized by Levene (135) it needs no further comment. However, for purposes of clarity in the following discussion, it may be pointed out that purines, like pyrimidines, may for convenience be arranged into groups depending upon the number of oxygen atoms present in the molecule and that, therefore, all compounds belonging to this general class may be referred to the following types:



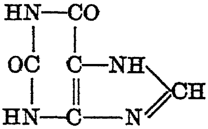
Purine

I



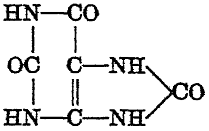
Hypoxanthine

II



Xanthine

III



Uric acid

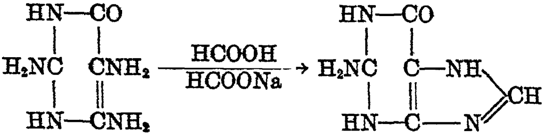
IV

These types retain their individuality even when oxygen has been replaced by sulfur or by imino groups and when the hydrogen has been substituted by hydrocarbon residues. These relationships having been definitely established, it is now possible to summarize briefly the methods which are applicable to the synthesis of these substances from pyrimidines.

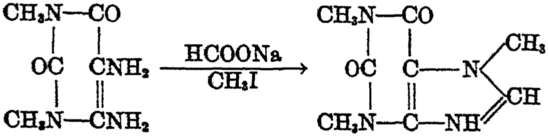
Such syntheses fall into two general classes if limited to methods which are capable of extended application: A, those involving the preparation of 5-aminopyrimidines (uramils, etc.), pseudouric acids, and the subsequent condensation of the latter; B, those involving the preparation of 4,5-diaminopyrimidines and their condensation under the action of different reagents. Of these two the latter is perhaps the more varied in its scope.

(A) Synthesis from 5-aminopyrimidines involves treatment of the substance with potassium cyanate with the formation of a substituted urea side chain in the 5-position. Such reactions usually take place readily. This is followed by the condensation of the urea side chain to form an imidazole ring. The ease with which the final phase in this process takes place varies greatly depending upon the character of the other substituents in union with the atoms of the pyrimidine ring. As has been noted in connection with the discussion of thiouramils, the presence of sulfur in the 2-position retards this reaction. Behrend has reported the same resistance to condensation in the case of the pseudouric acids obtained from 5-aminouracil and 4-methyl-5-aminouracil (10d, 11c, 13b, 14a). The unsuccessful attempts of Baeyer to synthesize uric acid from uramil have been referred to. In this case, however, the condensation of the urea side chain was ultimately effected by Fischer (38b) as a result of fusing pseudouric acid with molten oxalic acid. In studying condensations of this type Fischer later found that hydrochloric acid was very effective in bringing about this reaction. Even the pseudouric acid derivative of uramil when warmed with this reagent is transformed smoothly into uric acid. In the case of the corresponding methylated derivatives of uramil, the reaction is very much accelerated so that even dilute hydrochloric acid may be used to induce this change.

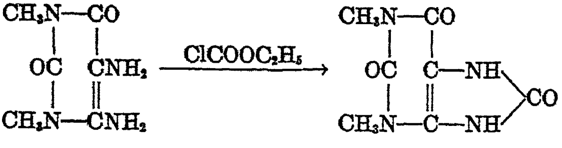
(B) Synthesis of purines from 4,5-diaminopyrimidines involves condensation with formic acid (in the presence of sodium formate) on the one hand, or with ethyl chloroformate or urea on the other. In cases where formic acid is used as the condensing agent an intermediate formyl derivative is frequently isolated, and the ease with which it suffers condensation to form an imidazole ring varies considerably with different compounds. The character of the imidazole ring depends upon the reagent chosen for the condensation, as is apparent from the following illustrations chosen at random (190 e, j, and k, respectively).



Guanine



Caffeine

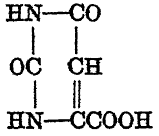


1,3-Dimethyluric acid

It may be added that by varying the character of the pyrimidine chosen the above methods of synthesis are applicable to the preparation of any purine belonging to the various groups classified under I, II, III, and IV (p. 286).

In conclusion, attention may again be directed to the fact that many important problems in biochemistry depend for their ultimate solution upon a knowledge of pyrimidine chemistry. This has already been pointed out in some detail in connection with a preliminary survey of the chemistry of the nucleic acids and also in the more recent discussion of the chemistry of the purines. But there are innumerable other illustrations of the fact that pyrimidines play a conspicuous part in both animal and plant metabolism. Indeed the whole development of pyrimidine chemistry during the past century has been interlaced with fundamental biochemical problems. For example, the synthesis of cytosine and isocytosine was undertaken because of the fact that a substance having this composition had been isolated as a degradation product of both plant and animal tissues. The successful synthesis of cytosine confirmed the constitution of the major aminopyrimidine occurring in quantity in the nucleic acid molecule. The fact that a substance having the composition of a monoöxydiaminopyrimidine was isolated by Kutscher (126) from among the hydrolytic products of yeast nucleic acid led to the synthesis of 2-oxy-4,6-diaminopyrimidine (199a), 2-oxy-5,6-diaminopyrimidine (103a), 6-oxy-2,4-diaminopyrimidine (190a; cf. 100g), and 6-oxy-2,5-diaminopyrimidine (100g). These four substances represent all of the molecular configurations that are possible for a compound of this composition and of these the last is the only one which agrees in its general chemical properties with Kutscher's base (100g). The fact that identification of these two substances has not yet been established is due in part to the fact that the product isolated from natural sources has not been thoroughly investigated.

Another illustration of the way in which pyrimidine chemistry has been applied to the elucidation of biochemical problems is to be found in the investigation of some of the many possible isomeric aminodimethylpyrimidines having the composition of a base which has been isolated from among the hydrolytic products of Japanese *Schōyu* (Soja sauce) (185, 184). Such a substance might represent a derivative of 2-, 4-, or 6-aminopyrimidine. The isomeric modifications corresponding to 4-amino- and 6-amino-dimethylpyrimidines have not as yet been completely surveyed. While all dimethyl derivatives of 2-aminopyrimidine have been carefully examined, none of these corresponds in its chemical properties with the base described by the Japanese investigators (106a; cf. 90a). The final solution of this problem is, therefore, one requiring further study. Another important development in the field of pyrimidine chemistry is the discovery that uracil-4-carboxylic acid synthesized by Wheeler (197) in 1907 has been shown to be identical with *orotic acid* found in milk (3).



Research developments in the field of pyrimidines have had of course their purely theoretical as well as their practical aspects. Gaps in the chemistry of different groups of compounds belonging to this general class are gradually being filled in and the importance of such work cannot be overestimated. Had it not been for the synthesis of the isomeric diaminodioxypyrimidines by Traube, the solution of the structural relations of divicine and vicine would have been very much retarded. 5-Methylcytosine was synthesized by Wheeler and Johnson many years before it made its appearance among the hydrolytic products of tuberculinic acid. Moreover, since some of the most important developments in biochemistry today are concerned with the so-called chemistry of the cell, it may be predicted with confidence that progress in the elucidation of the very complicated problems involved in this study will be associated in the future, as it has been in the past, with extended investigations in the field of pyrimidine chemistry.

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HELIUM AND THE PROBLEM OF GEOLOGICAL TIME[1]

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INTRODUCTION

Few branches of science have been developed with such rapidity as that of the phenomena of radioactivity. One would show a decided bias in mentioning any particular investigator or indeed any list of experimenters, which might be compiled in this limited space, who have worked in this field during the thirty-seven years since the discovery of the radioactivity of uranium by Professor Henri Becquerel. For a complete reference to all the literature on this subject the reader is referred to the excellent book on *Radioaktivitaet*, by Professors Stefan Meyer and Egon v. Schweidler (1), or for a brilliant modern discussion and particularly to those interested in the experimental side, *Radiations from Radioactive Substances*, by Rutherford, Chadwick, and Ellis (2). A comprehensive introduction to the subject is afforded by G. v. Hevesy and F. Paneth's *Lehrbuch der Radioaktivitaet* (3).

The first seven years were devoted to the compilation of a mass of facts, the chaotic nature of which was reduced to order by the application of the transformation theory of Rutherford and Soddy in 1903. It must here be assumed that the reader has knowledge of the theory of spontaneous disintegration of the radioelements accompanied by the loss of an α- or β-particle and the subsequent formation of the transformation series, three of which are known today. It was soon shown that such series end in definite stable products and that the time required to produce a given amount of the end-product of a given series from a given amount of the parent element is always the same once radioactive equilibrium has been established. Owing to the probability nature of the spontaneous disintegration this statement, however, must be modified so as not to include small intervals of time, measured in seconds and minutes. Stating this in mathematical terms, the disintegration constants of all the radioelements are invariable, at least under the ordinary physical conditions existing on the earth today. Radioactive equilibrium is attained when as many atoms of the "daughter element" disintegrate in a given time as are produced from the "parent element." On scanning the uranium series it will at once be seen from the average life of ionium, that a period of many thousands of years will be necessary for the establishment of equilibrium in the uranium series. In the case of the thorium series a few years is sufficient. With the actinium series in an uncertain state in the initial stages, this necessary period cannot be determined, but it is probably less than that required for the uranium series. The case of very young minerals and rocks will not be discussed here. The next progressive step was to show that one and only one α-particle was ejected on each successive transformation, except in the case of dual disintegrations and branching series. Determinations of the ratio of the charge to the mass of the α-particle by Rutherford and Soddy in 1903 (4) showed that the α-particle was probably a doubly positive charged helium atom. The association of helium with minerals containing uranium and thorium had been noticed previously by Ramsay, and in 1904 Ramsay and Soddy (5) found that helium was present in the gases released by heating or dissolving radium salts. The identity of the α-particle with the helium nucleus has long since been firmly established. It was correctly concluded in the early stages of the history of radioactivity that the β-rays consisted of high speed electrons.

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[1] Contribution No. 304 from the Massachusetts Institute of Technology.

The series

The end-products of the uranium and thorium series having been ascertained as lead, by tracing the various steps in the transformation series with the help of the radioactive displacement law, it was found that the uranium series should end in the lead isotope 206 and the thorium series in the isotope 208. Recent investigation by Aston (6) on the isotopes of lead would indicate that the isotope 207 is the end-product of the actinium series. It is now possible to draw up a diagram of the end-products of the three known disintegration series which under the condition of the attainment of radioactive equilibrium will illustrate the methods of determining the age of matter containing radioelements simply by reference to the initial radioelement and the final products. This is shown in figure 1.

The method of determining the age of a mineral from the proportion of uranium and lead present was first suggested by Boltwood (7). It has been necessary to modify Boltwood's method only in so far as he assumed that all the lead was produced by uranium. We now know that in addition to thorium and actinium lead, account must be taken of ordinary lead. Rutherford (8) was the first to draw attention to the helium method of determining the age of a mineral. Between 1905 and 1911 appeared a series of papers by R. J. Strutt (Lord Rayleigh) in which he worked out in detail the relation of the helium to the radioelements. A very complete résumé of these results is given in Bulletin No. 80 of the National Research Council, *The Age of the Earth*, or in Abegg's Handbuch (9).

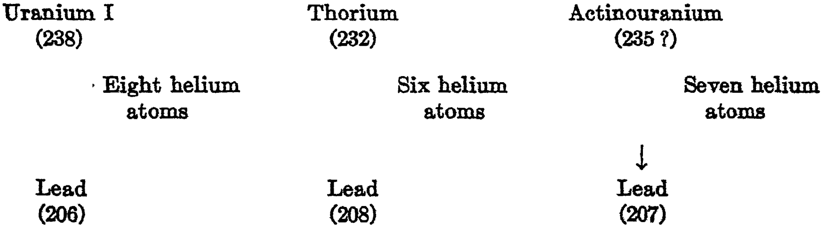


FIG. 1. THE END-PRODUCTS OF THE RADIOACTIVE SERIES

The fivefold test on the age of a mineral

From figure 1 it will be seen that if the possibility of common lead is excluded, and the amount of uranium, thorium, and actinium and the respective proportions of the lead isotopes determined, three independent ratios giving the age of the mineral can be obtained. Such determinations at present are very few and do not lead to very accordant results, but this is mainly due to the uncertainty of the constants in the less studied series of thorium and actinium. The accurate determination of the isotopes of lead is now within the range of possibility even on a large scale, as is shown by Aston's recent results (10). The fourth test is given by the ratio of helium to uranium, thorium, and actinium. The fifth test is the oxygen method proposed by A. C. Lane, on which no crucial calculations have been made as yet (see appendix). A sixth test might be added, namely, the study of the pleochroic haloes, which will be mentioned later, were it not that the present methods of determining the quantities to be known place this method far outside of the degree of accuracy with which the other tests can be applied. So far no fivefold test has been applied, with the possible exception of a uraninite (see appendix); the highest is probably a threefold test by the uranium, thorium, and helium ratio, but such tests lead at present to very discordant results, partly on account of the practical difficulties. Thus recent research has shown that the helium method is applicable only when exceedingly minute radioactivity is present, so that although the very small quantities of uranium and helium can still be measured with accuracy, the amount of lead present is far too small for a determination. For the present, therefore, each mineral will have to be treated appropriate to its analysis. Before discussing this problem, however, it may be well to consider the evidence for the constancy of disintegration of the radioelements.

THE SPONTANEOUS DISINTEGRATION OF THE ELEMENTS

Apart from the three series mentioned previously, so far only three other elements of the periodic system have been found to show an activity. Potassium and rubidium exhibit a weak activity, but no series associated with these disintegrations yielding only β-particles has been traced. G. v. Hevesy has lately found samarium to be radioactive, yielding probably an α-particle (11).

Artificial disintegration

Many are the experiments which have been carried out in efforts to alter the rate of disintegration of the radioelements or produce artificial disintegration. The effects of temperatures up to 3000°C. and pressures of 20,000 atmospheres, of very strong fields of electrical, magnetic, and gravitational type, have all failed to show a positive result. That such puny sources of energy would not avail might have been predicted from the quantum theory. Einstein has shown that the emission of radiation may be stimulated by incident radiation. To become effective, however, such incident radiation must closely approach in quantization the emitted radiation. Thus to remove electrons from the outer orbits is an everyday occurrence, but it requires many thousands to even millions of times this incident radiation to effect a nuclear rearrangement. The wave length of the radiation, λ, and the temperature, T, are found to be connected by the relation $\lambda T = 0.2885$ cm. deg. From this relation Jeans (12) has drawn up table 1 showing the mechanical effects of radiation. When some such temperature as 5.8×10^9 °A. is reached, but not before, the nuclei of uranium will commence to rearrange themselves.

The next obvious step to increase artificially the rate of disintegration was to bombard a radioactive element with a source of α-particles. Such a source would have an energy corresponding to about 6×10^{10} degs. in the case of the fastest. This however failed, and its failure is again predicted by the quantum theory on determining the probability of disintegration by α-particle bombardment for heavy elements. Jeans finally concludes that apart from the "white dwarf stars," whose center probably consists of only nuclei and free electrons—their density is enormous compared to matter in the earth—and the spiral nebulae, "No place is known hot enough to have any appreciable effect on the transformation either by synthesis or by disintegration, of the radioactive elements. . . ." It has been suggested that radioactive disintegration is effected by the penetrating or so-called cosmic rays. By measuring the activity of a polonium preparation at the bottom of a mine and at the surface, Maxwell (13) showed that such an effect must be less than 1 per cent. Another method has suggested itself to the author, namely, that the age of specimens taken from an inclined basaltic flow such as may be traced downwards for some thousands of feet in the Keweenawan copper mines should show differences even though the flow is definitely of uniform age, if the penetrating radiation is effecting the disintegration and the specimens are taken so as to have been exposed to the radiation in one set and not exposed in a second set. Some preliminary results which appear to show that no differences are exhibited have been obtained, but on account of their preliminary nature are withheld for future publication.

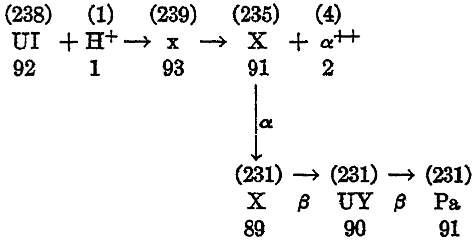
TABLE 1

The mechanical effects of radiation

Sir James Jeans

WAVE LENGTHS	NATURE OF RADIATION	EFFECT ON THE ATOM	TEMPERATURE	WHERE FOUND
cm.			*degrees A.*	
7500×10^{-8} to 3750×10^{-8}	Visible light	Disturbs outermost electrons	3850 to 7700	Stellar atmospheres
250×10^{-8} to 1×10^{-8}	X-rays	Disturbs inner electrons	115000 to 29,000,000	Stellar interiors
5×10^{-8} to 1×10^{-9}	Soft γ-rays	Strip off all or nearly all electrons	58,000,000 to 290,000,000	Central regions of dense stars
4×10^{-10}	γ-Rays of Radium B	Disturbs the nuclear arrangement	720,000,000	
5×10^{-11}	Shortest γ-rays	—	5,800,000,000	
1.3×10^{-13}	Highly penetrating radiation (?)	Annihilation or creation of proton and accompanying electron	2,200,000,000,000	

The recent experiments of Cockcroft and Walton (14) are of interest in that the disintegration rate of uranium is apparently increased by bombardment with high speed protons. It is difficult to conceive of the presence of such protons in the present physical state of the earth, but such a bombardment might well have occurred in the sun. The process appears to be the reversal of the bombardment of some elements by α-particles, in that the proton is absorbed and an α-particle emitted. The product of the bombardment of UI is therefore an isotope of protoactinium of mass 235. A conceivable initial transformation of the actinium series might then be represented as in figure 2. Moreover on account of the close genetic relation—the head of the actinium series is, however, no longer a uranium isotope—it might be expected to find a reasonably constant proportion at any given time of the uranium series to the actinium series, as is actually observed in a few analyses made. Such a mechanism must have ceased operation when the earth was born, otherwise we must postulate a source of protons of the required energy in the earth today. The necessity of accounting for any excess helium production by this and similar mechanisms, in age determinations, and the question of the large helium content of beryls has been discussed by Urry (15).



$$\begin{tikzcd} {}^{(238)}_{92}\mathrm{UI} + {}^{(1)}_{1}\mathrm{H}^{+} \arrow[r] & {}^{(239)}_{93}\mathrm{x} \arrow[r] & {}^{(235)}_{91}\mathrm{X} + {}^{(4)}_{2}\alpha^{++} \arrow[d, "\alpha"] & & \\ & & {}^{(231)}_{89}\mathrm{X} \arrow[r, "\beta"'] & {}^{(231)}_{90}\mathrm{UY} \arrow[r, "\beta"'] & {}^{(231)}_{91}\mathrm{Pa} \end{tikzcd}$$

FIG. 2. POSSIBLE MECHANISM OF THE FORMATION OF THE ACTINIUM SERIES

Pleochroic haloes

Perhaps the best positive evidence of the constancy of the rate of disintegration of the various radioelements is afforded in observations of the previously mentioned pleochroic haloes. The α-particles have certain characteristic properties, amongst which is the property to ionize all gases through which they pass and solid bodies in which they are absorbed. In certain minerals this property is exhibited by a permanent visual after-effect in the formation of concentric darkened or colored rings surrounding a minute radioactive inclusion. These darkened rings seen in a thin cross-section are really spheres in the body of the mineral or a succession of shells. The reason for the appearance of the ionization effect in rings and not as circular uniform dark areas lies in the fact that the ionizing power of an α-particle increases rapidly and reaches a maximum very near to the end of its "range," as may be seen from figure 3.

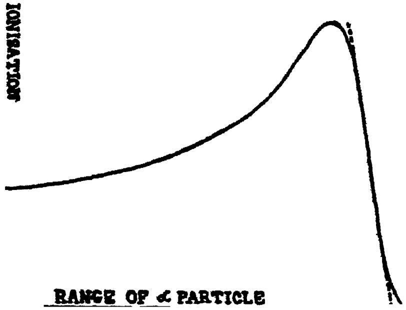


Fig. 3. Variation of the Ionizing Power of an α-Particle with Distance Travelled

The range of an α-particle in a given medium is a perfectly definite quantity for any given radioelement and has been found by Geiger and Nuttall to be connected with the rate of disintegration of the element producing the α-particle by the following relation:

$$\log \lambda = A + B \cdot \log R$$

where λ is the disintegration constant, A and B constants, the first of which depends on the series considered, the second being independent thereof, and R the range. Thus Joly found the maximum radius of the haloes referred to the uranium series in biotite to be about 0.04 mm., which agrees closely with 0.041

mm. found for RaC′ in biotite experimentally. The various other rings of smaller radius can be identified, at least in fluorspar, with those due to the other members of the series, but the center of the halo in biotite is usually more or less of even intensity owing to the combined, although small, ionization effect of all the α-particles in their initial excursions. Many observers have made measurements since the pioneer work of Joly, and the constancy of the radii of the various rings in both thorium and uranium haloes in minerals of all geological ages has led to the conclusion that the rates of disintegration of the radioelements have not altered during geological time. A very able summary of our present knowledge of these haloes is given by Arthur Holmes (16).

THE APPLICABILITY AND RELIABILITY OF THE LEAD AND HELIUM METHODS

In order to compare the two methods it is as well to summarize first the required data for a complete solution of the age determination for each case. Kovarik (17), in developing the formula for the exact determination of the age by the lead method, has clearly enunciated the conditions and requirements. He writes, "To be able to attack the problem successfully we must be reasonably sure that the mineral did not change by admixture from outside or by losses from inside and that only such changes have taken place as can be ascribed to radioactive disintegration. In addition we must have a knowledge of the following things:

(A). The data from the analysis of the mineral, namely, the masses of uranium, thorium, and lead (all isotopes) per given mass of the mineral.

(B). Atomic weight of the lead (all isotopes) from the same analysis.

(C). The disintegration constants of the radioactive elements involved.

(D). The atomic weight of the various lead isotopes, separately.

(E). The parental lineage of the various isotopes of lead.

(F). The possibility of the presence of common lead and of each one of the several lead isotopes separately at the time of formation of the mineral."

Minor difficulties present themselves in conditions C, D, and E, such as a lack of accurate knowledge of constants or of the origin of the actinium series, but the errors involved are often less than those in the data under A. Condition B presents difficulties in many of the older analyses, since no determination is available or, if so, probably from some second sample of the material.

Helium method

For the helium method the condition in Kovarik's opening paragraph above must also apply and a knowledge of the following:

(1). The data from the analysis of the mineral, namely, the masses of uranium and thorium and the volume of helium contained in a given mass of the mineral.

(2). The disintegration constants of the radioactive elements involved.

(3). The possibility of the presence of helium at the time of formation of the mineral.

The factors involved in the helium method are therefore but three in number compared to six in the lead method; moreover, condition 3, comparable to condition F in the lead method, is considerably simplified in that the only possibility involved in the helium method is a retention of helium from a previous formation, whereas in the lead method there is the possibility of the original formation containing the end-product isotopes in addition to ordinary lead, in which case the problem is insolvable without the analyses of many minerals of varied content but the same geological age. It has been customary in the past to base reliable age determinations only on specimens in which the lead has been found to have an atomic weight very near to 206 or 208, but this has been shown by Kovarik (17) still insufficient to satisfy condition F, particularly with regard to the common lead possibility, and the method certainly limits the field of application to a very few specimens (18). Now let us examine the evidence which throws light on condition 3 in the helium method. The so-called radioactive minerals containing between 0.01 and 50 per cent or more uranium may contain anything up to 10 cc. of helium per gram. Wood (19) has investigated the loss of helium from monazite and thorianite and his results are tabulated in table 2. Such minerals, however, are definitely out of the range of the helium method on account of a loss which also occurs merely on grinding and quite certainly occurs to a large extent over the periods of geological time. For reasons to be discussed below, the helium method is at present known to be applicable only to fine-grained rocks and minerals containing the order of 10^{-6} to 10^{-7} gram of uranium, a little more thorium, and hence about 10^{-4} to 10^{-8} cc. of helium. Such rocks and minerals have been found to lose nearly all of these small quantities of helium under the conditions of the formation of the rock, although the helium would appear to be closely held in the physical state of their present existence after the necessary cooling period. It is impossible to conceive of the small quantities of helium in the ordinary rocks as being the retained helium from heated highly radioactive and therefore high helium content minerals, since the radioactivity is infinitesimal compared with minerals which might conceivably retain these small quantities. It then remains only to consider the possibility of absorption of helium by the specimens to be worked with. If helium is absorbed by rocks on cooling and this absorption presupposes a source of helium in the neighborhood of the magma which must be greater than that in the atmosphere at present, then under the experimental conditions of liberating the helium from a rock, allowing it to cool in the atmosphere of its own evolved gases, pumping off these gases and reheating, the amount of absorption can be determined. It was found to be less than the detectable amount of helium, or $<10^{-10}$ cc. Paneth and Peters (20) found that the diffusion of helium through palladium was also less than this minimum detectable quantity at 1000°C. Similar unpublished results of the author are also included in table 2. The very small absorption of helium by potassium chloride is insufficient to support the proposal that absorption accounts for the high helium content of sylvin and carnallite found by Strutt (9). The non-absorption of helium by basalts at room temperature is illustrated in another experi-

TABLE 2

The liberation and absorption of helium

	EXPERIMENT	TEMPERATURE *degrees C.*	
Wood, O. D.	Liberation of helium from monazite containing about 9 cc. per gram	720 1000	68.6 per cent of total 98.3 per cent
	Liberation of helium from thorianite containing about 9 cc. per gram	750 1000	62.3 per cent of total 100.0 per cent
Urry, W. D.	Liberation of helium from a fine-grained Keweenawan basalt. Total content 11.73×10^{-5} cc.	900 1050	78 per cent of total 91 per cent
	The specimen, heated to 1050°C., was allowed to cool in its own evolved gases, whereupon it was found to give off on isolation and reheating......	1050	$< 10^{-4}$ per cent of the previous loss
Urry, W. D.	Diffusion of helium through bismuth 1 mm. thick; 4 hours	125	10^{-9} cc. of helium
Urry, W. D.	Diffusion of helium through copper 1 mm. thick; 4 hours	700	$<10^{-9}$ cc. of helium
Urry, W. D.	Diffusion of helium through iron 1 mm. thick; 4 hours	850	$< 10^{-9}$ cc. of helium
	(In the last three experiments the limit of detection was 10^{-9} cc. of helium.)		
Urry and Hettich	Potassium chloride was crystallized over a period of several months under one atmosphere of pure helium, removed and evacuated for one hour. Contained..............	18	5.7×10^{-8} cc. per gram
Urry, W. D.	Sliced specimen of Keweenawan basalt. Control half contained..........	26	11.71×10^{-5} cc. per gram
	Analysis of the second half after three months continuous exposure to 200 mm. Hg; pressure of helium during diffusion experiments gave.........		11.65×10^{-5} cc. per gram

ment. A fine-grained basalt from Keweenaw Point, Michigan, was sliced and cut into two parts. One part was fused for a helium determination and the second was used in the course of some diffusion experiments. Although quantities of the order of 10^{-4} cc. of helium passed through the rock, an analysis of this second specimen showed almost the same helium content as the first specimen. This experiment is interesting from several angles, for it tends to show that diffusion rates of helium as measured by the helium–mineral–vacuum method do not give us information as to the possible loss of helium from a rock. In this case the law of diffusion through fine capillaries was found to hold, and it is improbable that the diffusing helium entered the solid part of the rock at all. Again it is evidence that the radioactive helium is retained within the crystal structure and therefore that in the fine-grained rocks the radioactive points are not situated along the cracks as has been found for coarser rocks, for if such were so it is unlikely that the two results would have agreed.

Summing up the evidence in table 2 it would appear that there is small likelihood of the presence of helium at zero time of the age determination, namely, the time of solidification. Compared to the apparent ease with which this zero state of affairs is reached, the complete removal at the time of the formation of a mineral of the end-products, uranium and thorium lead, produced in the earlier history of its composite material, must depend upon volatility and chemical separation.

Limitations

Turning to Kovarik's introductory condition, it is obvious that although an age may be determined for a metamorphosed rock it has no particular significance. Metamorphism is the changing of the chemical and mineralogical composition, very often by oxidizing reactions or leaching by water or salt solutions. The proportional loss of the various radioactive elements and their end-products cannot be determined during this period, and the most that can be done is to assume that all the end-products were lost during the change, in which case the age gives us the time of metamorphism. Such an assumption can be made but rarely.

As far as the helium method is concerned, we have already dealt with the possibility of admixture from outside in considering the absorption of helium. It must here be noted that the diffusion rates of helium through glass and similar materials have no bearing on the diffusion of helium through crystalline substances. Thus Piutti (21) found that although he was able to detect with ease the diffusion through silica glass, he was unable to observe a diffusion through crystalline quartz. This experiment has lately been repeated by the author with a sensitivity of 10^4 times that of the above experiment, with the same result. The investigation of the diffusion of helium through glass, employing the most sensitive detecting arrangements so far possible, which has been carried out by Paneth and Peters (22) and lately investigated by Urry (23) in detail, although throwing light on the mechanism of such diffusion cannot tell us anything about the loss of helium from rocks and minerals and will lead to conclusions opposite to those found later to be correct. For this reason an investigation into the loss of helium from rocks etc., has been started by the author, and this will be dealt with under Kovarik's second condition. It has generally been argued, and in many cases correctly, that the inherent failure of the helium method of determining ages is due to a loss of helium from the inside; that helium being a gas cannot be retained throughout geological time in the same manner as lead. The conclusion that the helium method gave only minimum values was chiefly due to attempts to compare the lead and helium ratios. Since all the lead ratios must be of minerals of high radioactive and therefore of high helium content the comparisons are unfair, since it cannot be expected that there will be no loss of helium when the pressure of the generated helium may reach several atmospheres in the mineral.

Reliability

There is one class of substances which has the property of completely retaining the generated helium, namely, the metals. Paneth and Urry (24) have shown that the heating of the iron meteorites to 1000°C. for several hours will remove only the helium corresponding to the surface. The results of such experiments are shown in figure 4. A specimen of the iron meteorite Thunda was obtained from the British Museum, where it had existed for several years in the form of filings. The helium content derived from this sample was practically identical with that found for a compact piece of the same meteorite. It should also be noted that both Mount Ayliff and Thunda are the two meteorites containing the most helium of the forty-two so far investigated. It should be mentioned that the older method of liberating the helium by merely heating is far from sufficient. Thus in the case of the iron meteorite, Staunton, Augusta Co., Strutt recorded only about one-twelfth of the actual helium content found on dissolving the meteorite. Even in the case of the minerals, too great an uncertainty is introduced by assuming that a certain fraction of the helium is liberated at a given temperature. Many determinations have been nullified by such assumptions and the spurious results obtained have reflected on the helium method.

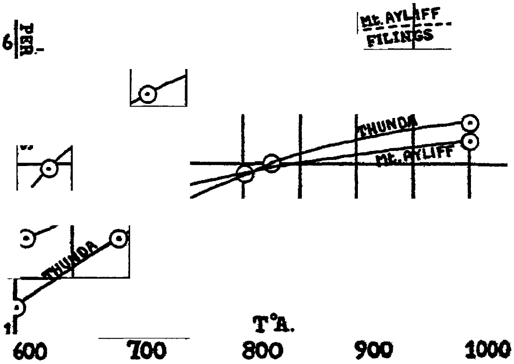


FIG. 4. THE PERCENTAGE LOSS OF HELIUM ON HEATING THE IRON METEORITES[2]

The determination of the ages of the meteorites and such native metals as may be found in the earth are decidedly of importance, but the limitations imposed by the rare occurrence of such material would detain us from making anything like a complete survey by this method. A stumblingblock has already been encountered in the case of the native metals, in that at least one has been found to contain an insufficient quantity of radioactivity, but there remains by far the greater proportion of such material for further work, especially in the field of native iron, silver, and gold. There has been found, however, of late another class of material that is likely to prove suitable for determinations by the helium method, namely, the fine-grained basalts, a class which it is highly important to investigate, since such material is abundant in every geological sub-period. The preliminary investigation of this material was undertaken by V. S. Dubey in collaboration with A. Holmes (25). The results are grouped together in table 3 to show the present limits of the applicability of the method in this class of rocks, together with some later determinations by Dubey (26). The helium measurements of these rocks, which necessitated the improvement of the technique to determine the ten to hundred-thousandth part of the helium ordinarily found in the "radioactive minerals," were made in the laboratory of Professor F. Paneth and the uranium and thorium determinations by Professor Mache's methods in Vienna. Owing to possible inhomogeneity of the specimens, all the measurements are now to be made on one sample in the same laboratory, which will remove a certain doubt of the results obtained from measurements of the three required factors on different samples.

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[2] In figure 4, "T°A" should read "T°C".

In discussing the results, A. Holmes (27) points out that specimens 1 and 2 are of a cryptocrystalline nature, which probably accounts for the apparent loss of helium, the ages being low. No. 3 is a fresh fine-grained rock yielding a value which may be expected to be about correct. No. 4 is definitely younger than No. 3 and the age is consistent with this. No. 5 is also consistent with the known geological period of the Whin Sill but may be 25 per cent low in the light of evidence from the lead ratios. It is interesting to note that the total lead content, including common lead, is about sixty times the expected radioactive lead. In Dubey's later determinations No. 1 is fine-grained and Nos. 2 and 3 progressively coarser, pointing to a reliability only in the case of the fine-grained, where the age is consistent with the lead ratios for the period usually assigned to the Gwalior series, al-

TABLE 3

The age of igneous rocks

GEOLOGICAL AGE	ROCK	LOCALITY	$He \times 10^6$	$Ra \times 10^{14}$	$Th \times 10^6$	AGE IN MILLIONS OF YEARS
			cc. per gram	*grams per gram*	*grams per gram*	
1. Miocene	Acid Felsite	Mt. Pawagarh plug, 100 ft. below summit, India	11.0	224.4	41.0	5
2. Miocene	Acid Felsite	Mt. Pawagarh plug, summit	10.0	224.4	31.0	5.9
3. Early Eocene	Nonporphyritic basalt, Deccan traps	Mt. Pawagarh, India (about 1400 ft.)	11.6	44.9	5.4	37
4. Oligocene or Miocene	Porphyritic tholeiite of the Cleveland dyke	Bolam, Co. Durham, England	11.0	62.2	6.1	28
5. Late carboniferous	Quartz-dolerite of the Whin Sill	Scordale Beck, Westmoreland, England	36.0	27.5	3.0	196
1. Late Precambrian	Fine-grained basalt flow	Belaki-Bauri, Morar group, Gwalior series, India	55.0	17.4	1.7	500
2. Late Precambrian	Medium-grained dolerite sill	Santowa Temak, Morar group, Gwalior series, India	42.0	17.5	1.5	389
3. Late Precambrian	Coarser grained dolerite sill	Panier, Morar Group, Gwalior series, India	31.0	21.1	2.4	203

TABLE 4

Illustrating the non-loss of helium from the fine-grained basalts

Part I. Analysis of the gases after sealing up specimens in pure oxygen for three months

SPECIMEN NO.	OXYGEN PRESSURE	LOCALITY OF SPECIMEN	WEIGHT AND SURFACE	ANALYSIS AFTER THREE MONTHS	MAXIMUM HELIUM LOSS FROM ROCK	HELIUM LOSS PER YEAR PER GRAM	LOSS PER 100 YEARS AS PER CENT OF TOTAL CONTENT
	mm.						
11	453	Fine-grained basalt, Keweenaw	8 grams, about 13 sq. cm.	About 10^{-8} cc. of He + Ne in the air ratio	10 per cent of He in the foregoing mixture $= 2.5 \times 10^{-10}$ cc.	1.1×10^{-10} cc.	0.05
25	671	Mesnard epidote, Felsite	8 grams, about 12 sq. cm.	About 10^{-8} cc. of He + Ne in the air ratio	As above $= 2.5 \times 10^{-10}$ cc.	1.1×10^{-10} cc.	0.03

Part II. Analysis of piece and powdered specimens of a Keweenawan basalt

SPECIMEN NO.	LOCALITY	REMARKS	EXPERIMENT AND NO.		TOTAL HELIUM CONTENT ON FLUXING
					cc. per gram
23	91st level of No. 2 shaft, Quincy mine, Keweenaw Point, Michigan	Highest helium content of twenty Keweenawan basalts	1	1.96 grams in one piece	38.98×10^{-5}
			2	1.96 grams in nineteen pieces	38.90×10^{-5}
			3	1.96 grams finely powdered	39.34×10^{-5}

though no lead ratio for material from this site is available. In the first report of this work (25), Holmes writes, "Clearly there is a large field of geological research now open to investigation by the long-neglected helium method. If our initial hopes are realized—and these preliminary results provide ample encouragement —a method is now available for dating all fresh igneous rocks which have not been heated up or metamorphosed since they came into place. . . . . Moreover, since igneous rocks suitable for the helium method are far more abundant and far better distributed in time than are radioactive minerals suitable for the lead method, there is now available a practical means of effecting long distance correlations and of building up a geological time scale which, checked by a few reliable lead ratios here and there, should become far more detailed than could ever be realized by means of the lead method alone."

During the course of an investigation of the Keweenaw series of Michigan, which is still in progress, the writer has found evidence supporting the reliability of the helium method for the fine-grained basalts. Thus one specimen, No. 23 from the bottom of the Quincy mine, was found to give repeatedly the same helium content whether a single piece was taken or a finely powdered specimen, thus exhibiting no loss of helium on grinding. Certain specimens were sealed up in a helium-free, that is, an air-free, oxygen and an analysis made of the gas after three months. Table 4 gives the combined results and the evidence for the retention of helium under the existing conditions. It will be seen that the analysis showed both helium and neon in the proportion in which these two gases are found in the atmosphere. Such sealing up experiments usually give this result, owing to the occlusion of air. This does not invalidate the experiments as a maximum value, for the leakage can still be obtained. The proportion of helium to neon in the atmosphere is approximately 1 to 3. Thus the amount of helium in the analysis above is $< 2.5 \times 10^{-9}$ cc. A variation of 10 per cent of the helium from the proportion in the air could have been detected spectroscopically and thus the maximum amount of helium having its source in the rock must have been 2.5×10^{-10} cc. From the last column it will be seen that specimens similar to these would yield reliable age determinations even after exposure to the atmosphere for one hundred years or more. The rate of loss of helium from the same rocks *in situ* must be far less than the above determined maximum rates on small samples with exposed surfaces and reduced pressure conditions. In connection with the helium results for specimen No. 23 it is interesting to note that, assuming a complete loss of helium on denudation of the surface rocks, the atmosphere contains today only a fraction of the helium which would have been set free, or, conversely, the denudation required to produce the atmospheric helium is absurdly small. The retention of helium on grinding such rock as the Keweenawan basalt is probably an explanation of this difficulty, since we can now assume that, at the most, only a fraction of 1 per cent is given off in the denudation of a large proportion of the surface rock.

Analytical limitations

Finally we have to consider Kovarik's condition A, namely, the data from the analysis, and with this condition also the fact (B) that the atomic weight of the lead from the same analysis shall be known. The lead method is immediately limited to the radioactive minerals, not on account of the uranium and thorium analyses which can be accomplished even when these elements are present in too small amounts for chemical detection, but on account of the lead determinations and more so since the atomic weight of this lead must be known. Thus to take the example of an iron meteorite which contains on the average 10^{-7} to 10^{-5} cc. of helium (this can be determined with an accuracy of 1 per cent (28)), this amount corresponds to the formation of 10^{-10} to 10^{-8} gram of lead. The radioactive lead, however, must be accompanied by a far greater amount of common lead, for I. and W. Noddack (29) have found on the average 5×10^{-5} gram of lead per gram of meteorite, and for the present it is quite impossible to determine the lead isotopes in such a mixture. As we have seen with the Whin Sill, such a state of affairs also exists in the ordinary rocks, and thus the lead method is limited to minerals containing sufficient lead for both the ordinary and isotopic analysis and in which all Kovarik's conditions can be satisfied, a limitation which seriously hinders the setting up of a complete geological time scale. On the other hand, analysis leads to no such limitations for the helium method, unless it be that certain minerals contain less than the detectable amounts of radioelements and helium. Only two substances have so far been found limited by this extremity. The Keweenawan copper was found by Paneth and Koeck (30) to contain $< 10^{-15}$ gram of radium per gram, as also was the iron meteorite Savik. With regard to the last it is no longer necessary to account for the absence of helium by assuming a passage near the sun (31), since it is merely due to the absence of radioactivity. The helium method is limited for quite another reason, which was given above. For the present it may be said, aside from the metals, to apply strictly only to the fine-grained lavas containing not more than about 10^{-4} cc. of helium per gram. Unfortunately, on account of the analytical difficulties, there remains a gap between the limits of the two methods, otherwise it would be possible to proceed by the two methods on one and the same suitable sample and thus to reconcile the methods. The lead method is at present limited to specimens containing at least about 0.01 per cent of lead, 0.3 per cent of uranium, and 0.5 per cent of thorium. Herein lies the difficulty of applying the fivefold test previously referred to.

THE DEVELOPMENT OF THE EXPERIMENTAL TECHNIQUE

The measurement of the helium content

In the field of detection and measurement of small quantities of helium, must first be mentioned the work of Soddy (32), who was able to detect 1×10^{-6} cc., followed by the studies of Strutt (Lord Rayleigh) (33), which have previously been mentioned, who was able to detect half this amount. This remained the limit of detection for several years, until the methods of Paneth and Peters (22) were published in 1928. These workers succeeded in detecting quantities of helium or neon as small as 10^{-10} cc. Finally Paneth and Urry (28) devised a method of accurately measuring quantities of helium of the order of 10^{-8} cc. This is practically the limit of the helium content of any geological material. The final form of the analysis apparatus is represented in figure 5. The principle of the purification process is to remove all the extraneous gases by adsorption on charcoal at liquid air temperature. At the partial pressure of the helium and neon in these experiments the adsorption at this temperature is quite negligible, whilst hydrogen is also incompletely adsorbed, necessitating its removal by chemical means. No attempt is made to separate the helium and neon, as the presence of neon is an excellent indicator of the former presence of air and in fact is made use of in the control experiments to determine qualitatively and quantitatively the possibility of error due to the presence of air and a consequent source of extraneous helium. Neon has a valuable asset in being capable of spectroscopic detection in a helium–neon mixture when present only to the extent of a few thousandths of 1 per cent. When present in greater amount the result is usually rejected. The refinements introduced by Paneth and Peters consist essentially of: (1) obtaining the helium or the helium–neon mixture in a pure state and therefore not having to detect these gases spectroscopically in the presence of other gases; (2) the avoidance of another source of extraneous helium than the presence of air, namely, by diffusion through heated portions of the glass apparatus; (3) producing the best conditions for a spectroscopic analysis by observation of the excited gas (using an external electrode) in the very small capillary attached to the McLeod gauge A.

The first refinement requires the chemical removal of the incompletely adsorbed hydrogen. This is best accomplished when present in large amount by absorption on fine calcium turnings heated to about 350°C. in the calcium oven B. In order to remove very small traces of hydrogen, the calcium oven is shut off from the rest of the apparatus, and after introducing a few millimeters of absolutely air-free electrolytic oxygen these traces are burnt over heated palladium at about 300°C. in the palladium oven C, so constructed that by alternately cooling and warming the charcoal D a to and fro circulation of the gases over the palladium is obtained. The final stage in any analysis is the adsorption for one hour on charcoal D, which is then shut off, and a further adsorption for two hours on charcoal E, whereupon the McLeod gauge is run up and the spectroscopic and quantitative analysis made. The method of vacuum jacketing the heated ovens and further immersing them under water should be noted in figure 5. This is the second important refinement, being the method of obviating the diffusion of helium through hot glass (23). The winding of the heating elements on asbestos is also excluded, since such mineral has been found to contain appreciable amounts of helium. The McLeod gauge is constructed to measure directly the volume of helium in the capillary, which is of a diameter chosen according to the amount expected. In dealing with very minute quantities it may be as small as 0.1 mm. The

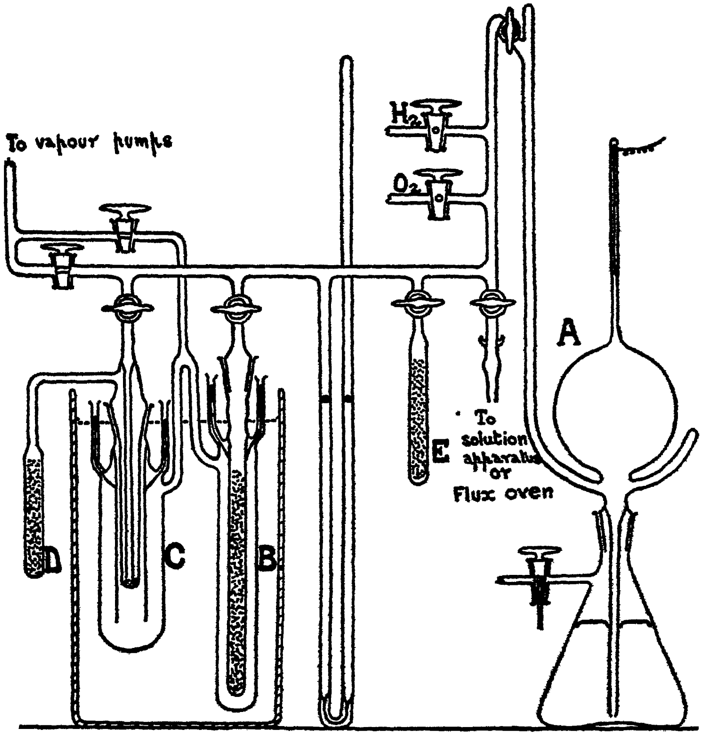
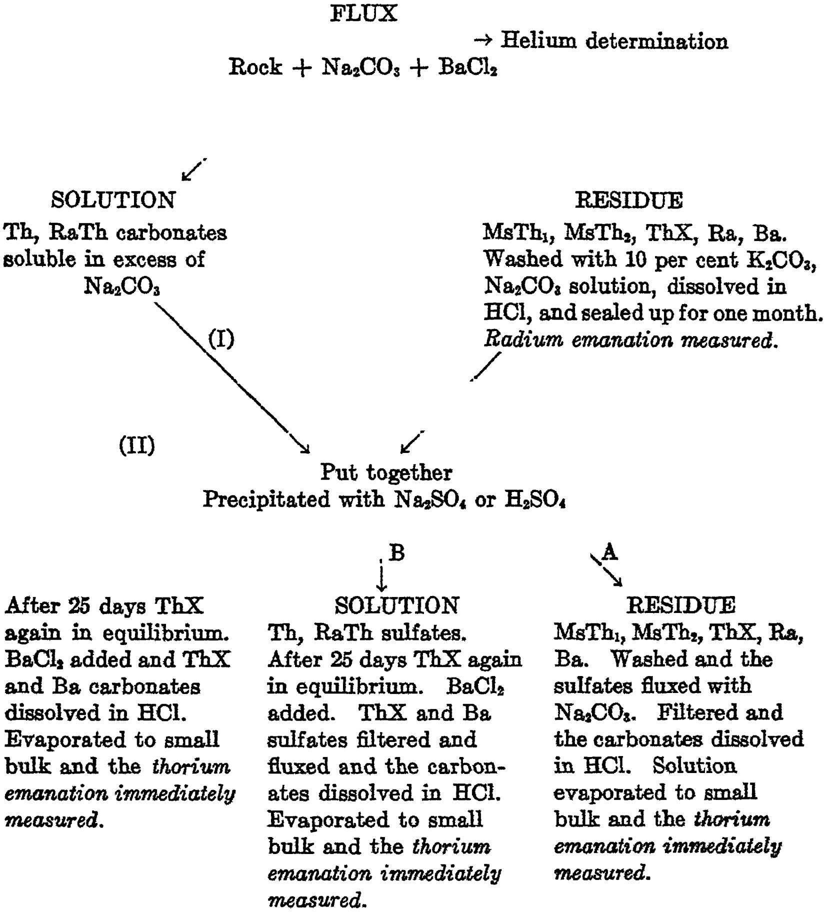


FIG. 5. DIAGRAM OF THE APPARATUS FOR THE DETERMINATION OF HELIUM

time for an analysis varies considerably with the mineral under investigation. Thus in the case of the solution of an iron meteorite in hydrochloric acid a large quantity of hydrogen is evolved, which conveniently acts as a carrier gas for the helium but which must be completely absorbed on the calcium. For a description of the apparatus for the solution of such soluble material under completely air-free conditions, the reader is referred to the original publication (24). In the case of insoluble material the usual procedure is to make a flux in a vacuum oven at 1000°C. and either to use the carbon dioxide available from the flux as a carrier gas or to supply air-free carbon dioxide conveniently formed by heating a powdered mixture of potassium dichromate and sodium carbonate. Since the type of vacuum oven is still a matter for further work it will not be depicted here.

The measurement of the uranium and thorium content

In order to determine the age of a rock, two further measurements are necessary,—the uranium and thorium content. Except in the case of the acidic rocks where the radioactive content is high compared to the basalts and meteorites, the difficulties of these measurements are even greater than the determination of the helium. The only practical method for the determination of these very small radioactivities is the emanation method. Thus if radioactive equilibrium has been established the measurement of the amount of any one of the series is sufficient to establish the content in any other of the radioelements of that series, the equilibrium amounts of each being known from their disintegration constants. Practically, the method involves the separation of the parent radioelement of the emanation of that series, the collecting of all the emanation in equilibrium with this separated parent in a suitable ionization chamber and the measurement by a comparison method of the emanation so collected. Figure 6 illustrates one possible series of chemical treatments which has been used, starting from the flux of the rock which may be conveniently carried out for the helium determination. All vessels employed and all reagents are treated previously with barium chloride to remove traces of sulfate which will precipitate the radium in a form not suitable for the complete recovery of the emanation. In most cases it is also necessary to treat the reagents by various processes to remove a certain activity which they



FLUX

→ Helium determination

Rock + Na_2CO_3 + $BaCl_2$

SOLUTION

Th, RaTh carbonates soluble in excess of Na_2CO_3

(I)

RESIDUE

$MsTh_1$, $MsTh_2$, ThX, Ra, Ba. Washed with 10 per cent K_2CO_3, Na_2CO_3 solution, dissolved in HCl, and sealed up for one month. *Radium emanation measured.*

(II)

Put together

Precipitated with Na_2SO_4 or H_2SO_4

B

A

After 25 days ThX again in equilibrium. $BaCl_2$ added and ThX and Ba carbonates dissolved in HCl. Evaporated to small bulk and the *thorium emanation immediately measured.*

SOLUTION

Th, RaTh sulfates. After 25 days ThX again in equilibrium. $BaCl_2$ added. ThX and Ba sulfates filtered and fluxed and the carbonates dissolved in HCl. Evaporated to small bulk and the *thorium emanation immediately measured.*

RESIDUE

$MsTh_1$, $MsTh_2$, ThX, Ra, Ba. Washed and the sulfates fluxed with Na_2CO_3. Filtered and the carbonates dissolved in HCl. Solution evaporated to small bulk and the *thorium emanation immediately measured.*

FIG. 6. THE CHEMICAL SCHEME FOR THE HELIUM-RADIUM-THORIUM ANALYSIS OF A ROCK

themselves contain. The separation depends upon the isotopy of the various radioelements. Thus, having obtained the carbonates of the two mesothoriums, thorium X, and radium in an excess of barium carbonate as a carrier there remains in solution the carbonates of thorium and radiothorium, the parent element of thorium X. The diagram explains the method of obtaining the equilibrium amount of emanation. If we are satisfied that the radiothorium went completely into solution, then after about twenty-five days we may proceed to obtain the thorium X, which is the parent of the thorium emanation by route II. The half-period of thorium X is 3.64 days, hence the period of several days required to reach equilibrium again after separation. As a control, however, this solution and that used for the radium determination may be put together, a sulfate added, and the thorium and radiothorium soluble sulfates separated out (route I). After the required period the solution is treated as under B. If, on putting the two solutions together, a time of twenty-five days is allowed to elapse before precipitating, the precipitate will again contain the equilibrium amount of ThX and can be treated as under A. The thorium emanation having a half-life of 54.5 seconds, equilibrium is quickly established, but once having obtained the ThX separated from its parent, the measurement must be made quickly on account of the short life of the ThX itself. If the much more slowly generated radium emanation affects the determination of the thorium emanation, the methods A and B should differ. When an acid solution is obtained after the helium analysis, this may be used directly for the radium determination and further treated in a similar manner as outlined above for the measurement of the thorium. If the radiothorium solutions after separation are kept for several months a correction must be made for the disintegration, since the half-life of this radioelement is 1.90 years.

Measurement of the emanation

The practical methods employed fall roughly into three classes, the order of which also corresponds with the historical order. The first method is that in which one ionization chamber is employed and the charge attained by the needle is progressively followed over a given period with some type of electroscope or electrometer. There is, however, present a natural ionization due to a variety of sources, chief amongst which is the local gamma radiation and the secondary effects at the walls of the chamber with penetrating radiation playing a small part as well. This natural ionization can be reduced to a minimum by taking various precautions, but there is a practical limit. When the ionization due to the emanation and its disintegration products is of the same order as the natural ionization the determinations become far too uncertain, especially since there is always doubt as to whether the natural ionization has remained the same during the period that must elapse between the control experiment and the measurement. In order to overcome this difficulty Halledauer (34) set up two identical chambers, the one containing the emanation and the other a control, so operated that the needles of both were allowed to charge up almost simultaneously for a given time, a slight difference in simultaneity being necessary to allow time to take the electrometer reading by the charge-sharing method, using the same electrometer for both chambers. Paneth and Koeck (30) have considerably modified this method, so that with quantities of from five to ten grams they were able to measure with a moderate degree of accuracy the minute radium content of the iron meteorites. The charge-sharing method

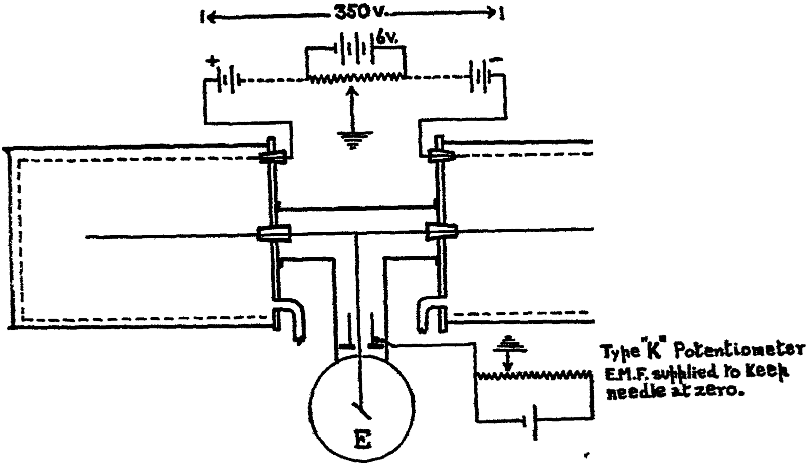


Fig. 7. Diagram of the Arrangement of the Apparatus for the Determination of Radium

has the disadvantage of requiring a very careful distribution of the various mechanical parts and exacting manipulation precautions in order not to change the capacities of the systems. The logical outcome of the above method was the development of the compensated system, which is shown diagrammatically in figure 7. The net arrangement used reduces the secondary effects at the walls, and the method of charging the ionization chambers oppositely cancels out the natural ionization, since the cause of this ionization must act equally on both chambers. This method also has the advantage of being able to apply a known voltage to a small ring condenser sufficient to keep the electrometer always at zero, thus eliminating leak errors.

On account of the very different life-periods of the radium and thorium emanations, different experimental procedures are necessary. Whereas in the case of the radium emanation it is sufficient to collect the whole in the chamber, with the thorium emanation the radioactive deposits of thoron must be collected by streaming through the solution containing the ThX, at a given rate for a given time. The ionization due to the deposits is then determined, the apparatus having been standardized by the same method with the active deposit from a known solution. Unlike the helium investigation, the measurement of radium in rocks has not been confined to a very few investigators, so that quite a detailed study of the distribution of radium can be made, whereas but few results are available for the helium content.

THE CALCULATION OF THE GEOLOGICAL AGE

The disintegration of the radioelements is a spontaneous process and as such may be written mathematically as:

$$N = N_0 e^{-\lambda t} \tag{1}$$

where N is the number of atoms left after time t, N_0 being the original number present, and λ the disintegration constant. After a time t let N' be the number of helium atoms produced since zero time. Since there are seven other elements yielding α-particles in equilibrium with uranium, N' is equal to $N''/8$

where N'' is the measured number of helium atoms. Thus we have

$$N' = \frac{N''}{8} = N_0 - N = N_0\,(1 - e^{-\lambda t}) \tag{2}$$

From equations 1 and 2 we have

$$e^{\lambda t} = \left[1 + \frac{N''}{8N}\right] \tag{3}$$

or, taking logarithms,

$$t = \frac{2.303}{\lambda}\log_{10}\left[1 + \frac{N''}{8N}\right] \tag{4}$$

The question of the value to be taken for λ_U is not such a matter for discussion as the choice of λ_{Th} treated below, since most of the determinations of the constant for uranium at least, agree fairly well. The value here employed is that chosen by Kovarik in his calculations (17), namely $\lambda_U = 1.52 \times 10^{-10}$ yr^{-1}. The helium value obtained in cubic centimeters per gram and the uranium in grams per gram must be converted into number of atoms, and the equation may be further reduced to the corresponding expression in terms of radium by including the factor found for radium to uranium of 3.40×10^{-7} under equilibrium conditions. We then obtain:

$$t \text{ (in years)} = 1.515 \times 10^{10} \log_{10}\left[1 + \frac{4.518 \times 10^{-10}\,\text{He}}{\text{Ra}}\right] \tag{5}$$

This formula may be reduced to the following approximate equations:

$$t \text{ (in years)} = \frac{\text{He}}{\text{U}} \times 8.8 \times 10^{6} = \frac{3 \times \text{He}}{\text{Ra}}$$

All the ages here given have been calculated by the exact formula 5. The above approximate formulas do not take into account the wearing out of the uranium. The ages of the iron meteorites as quoted by Holmes (35) were inadvertently corrected for this wearing out, and since they were originally obtained by the use of equation 5 the original data are correct. The error introduced by the use of the approximate formulas is usually within the experimental error for material less than about 300 million years old. Unlike some of the minerals used in the lead method, the rocks and minerals suitable for the helium method invariably contain thorium. Thus the age calculated by equation 5 will be a maximum, and to the radium in the denominator of the bracketed portion must be added the uranium equivalent, for the generation of helium, or the thorium present also reduced to terms of radium. Table 5 indicates the necessity for the determination of thorium.

TABLE 5*

The effect of varying proportions of thorium to the uranium present in lowering the age determined from the radium only

$\frac{Th}{U}$	AGE IN MILLIONS OF YEARS FROM EQUATION 5		
	550	1296	2174
	per cent	*per cent*	*per cent*
0.25	4.9	4.5	4.2
0.50	8.9	8.3	8.0
1.00	16.5	15.7	14.9
2.00	28.4	27.2	25.9

* This table was compiled assuming $\lambda_{Th} = 0.42 \times 10^{-10}$ yr^{-1}. A revision of the choice of this constant will be discussed below.

A preliminary survey shows that the proportion of thorium to uranium present in the iron meteorites is such that the values given in table 7 may be expected to be at the most about 10 per cent too high through neglecting thorium. In the rocks, however, the ratio is probably between 1.0 and 3.0 and possibly higher, hence to obtain any result even approximating the correct age thorium must be measured. Bearing in mind that the thorium series yields only six helium atoms compared to eight from the uranium series and that the rates of disintegration are different, the equivalent of thorium in terms of radium is given by,

$$\text{Th/Ra} \quad \frac{6 \times 238.14 \times \lambda_{Th}}{8 \times 232.15 \times \lambda_U} \times 3.40 \times 10^{-7}$$

The difficulty arises in the choice of λ_{Th}. Rutherford and Geiger (36) by the counting method found $\lambda_{Th} = 5.33 \times 10^{-11}$ yr^{-1}. Kirsch (37) by quite another method has found a value of 4.2 $\times 10^{-11}$ yr^{-1}. Kovarik deduces a probable ratio of 3.85 from some of Kirsch's later work. This corresponds to a value of 3.95 $\times 10^{-11}$ yr^{-1}. Taking Rutherford and Geiger's value the equivalent factor becomes 9.17×10^{-8} Th (expressed in grams per gram), or using Kirsch's result 7.23×10^{-8} Th. The full equation is then:

$$t \text{ (in years)} = 1.515 \times 10^{10} \log_{10}\left[1 + \frac{4.518 \times 10^{-10}\text{He}}{(\text{Ra} + 9.17 \times 10^{-8}\text{Th})}\right] \tag{6}$$

The error involved in this uncertainty of λ_{Th} will naturally increase with increase in the proportion of thorium present. Thus for the ratio Th/U = 1/2, a difference of 2.2 per cent in the age is found between the above two values of the equivalent factor. This rises to 3.8 per cent for the ratio Th/U = 1 and to 5.3 per cent for the ratio 2. In most cases this error will be less than the experimental error.

The effect of the inclusion of the actinium series with the uranium series

The work of Aston (6), Fenner and Piggot (18), Rutherford (38), and recently v. Grosse (39) shows that the origin of the actinium series may be not a branching of the uranium series but a start from an isotope of uranium. If this isotope were to disintegrate at a very much greater rate than UI, then we might expect, even though it is present in only a very small amount, a considerable discrepancy in the age. It can be shown that such is not the case, however. The measured uranium will consist of UI and actinouranium. We have then:

$$\text{UI} + \text{AcU} = \text{U} \tag{7}$$

If we designate the helium from UI as H_U and from AcU as H_{Ac} then:

$$H_U + H_{Ac} = \text{He (total)} \tag{8}$$

v. Grosse has found that, independent of any variables, the activity ratio of the actinium to the uranium series is 0.04. Thus we have:

$$\frac{\text{AcU}}{\text{UI}} = 0.04 \frac{\lambda_{\text{UI}}}{\lambda_{\text{AcU}}} \tag{9}$$

From equations 7 and 9 we get:

$$\frac{\text{U}}{\text{UI}} = 1 + 0.04 \frac{\lambda_{\text{UI}}}{\lambda_{\text{AcU}}} = 1.0034 \tag{10}$$

From the radioactive law we have:

$$\text{UI} = \text{UI}_0 e^{-\lambda_{\text{UI}} t} \tag{11}$$

$$\text{AcU} = \text{AcU}_0 e^{-\lambda_{\text{AcU}} t} \tag{12}$$

In a similar manner to the derivation of equation 3 and remembering that the uranium series gives eight α-particles to the actinium seven we have:

$$\text{H}_{\text{U}} = 8\text{UI}(e^{\lambda_{\text{UI}} t} - 1) \tag{13}$$

$$\text{H}_{\text{Ac}} = 7\text{AcU}(e^{\lambda_{\text{AcU}} t} - 1) \tag{14}$$

From equations 9, 13, and 14 we have:

$$\frac{\text{H}_{\text{Ac}}}{\text{H}_{\text{U}}} = \left[\frac{7}{8} \times 0.04 \times \frac{\lambda_{\text{UI}}(e^{\lambda_{\text{AcU}} t} - 1)}{\lambda_{\text{AcU}}(e^{\lambda_{\text{UI}} t} - 1)}\right] = r \tag{15}$$

Taking logarithms in equation 13 and combining with equations 15 and 8:

$$\frac{2.303}{\lambda_{\text{UI}}} \log_{10} \left[1 + \frac{\text{He (total)}}{8\text{UI}\,(1 + r)}\right] \tag{16}$$

A. C. Lane, in an address to the Annual Meeting of the American Mineralogical Society (1932), has pointed out that the disintegration constant of uranium as measured is that of the sum effect of UI and AcU, they being isotopes. Knowing this value and the tentative value of $\lambda_{\text{AcU}} = 1.73 \times 10^{-9}$ yr.$^{-1}$ as found by v. Grosse (39), and the activity ratio of 0.04 we obtain for λ_{UI} a value of 1.466×10^{-10} yr.$^{-1}$. This value has been used in equation 10 to find U/UI = 1.0034. Putting in this value to replace the unknown UI by U, the appropriate constants to reduce the uranium and helium to grams and cubic centimeters per gram respectively, and the U/Ra ratio, the final equation is:

$$t = 1.571 \times 10^{10} \log_{10} \left[1 + \frac{4.518 \times 10^{-10}\ \text{He}}{\text{Ra} \times 0.9966\ (1 + r)} \right] \qquad (17)$$

For instance, with a helium–radium ratio of 5 × 10^{-8} using equation 5 we find an age of 1340 million years. It will be noticed that the term t occurs in the value of r (equation 15). We can, however, employ the value of t from equation 5 to evaluate r. t is then determined for the same He/Ra ratio from equation 17, r redetermined, and a new value of t found. By repeating this process the final value of t which fits equation 17 is found to be 1263 million years, or 5.75 per cent lower than that calculated when the effect of the actinouranium is not taken into account. Moreover, by changing the activity ratio and the disintegration constant considerably, the percentage difference is not greatly altered. This is due to the presence of actinouranium being partly taken into account in equations 5 and 6 by the use of the disintegration constant of the mixture of UI and AcU. As the proportion of thorium increases, the error in neglecting to treat the problem by equation 17 becomes smaller. Having regard to the present accuracy of the analyses, equation 6 may be used especially for the younger rocks and minerals.

THE RESULTS

The age of the meteorites

The first determinations of the age of the meteorites were made by Paneth, Gehlen, and Guenther (31) in 1928. The helium was determined by the method here described, but the measurements were made by the McLeod method. The radium contents are those given by Halledauer (34) except in the case of Toluca, which was determined by Quirke and Finkelstein (40). Table 6 gives the results of the preliminary investigation. The average radium content of the meteoric types is given by Urry (41) as; iron, 2.5 × 10^{-14}, pallisitic (stone and iron) 7 × 10^{-14}, stony (Chondritic) 12 × 10^{-14}, and achondritic 20 × 10^{-14} gram per gram.

Owing to the possible inhomogeneity previously mentioned it was at once seen necessary to make the complete analysis on one and the same sample. Accordingly the Halledauer method and later the compensated method of measuring these border line radium contents was developed by Paneth and Koeck (30), and the accurate measurement of helium by a modified Pirani-Stern manometer system was worked out by Paneth and Urry (28) in the same laboratory. In table 7 both measurements are made on the same sample. The necessity for the analysis on the same sample is brought out in table 8, where the helium contents of some of the accessory minerals of the iron meteorites and of the iron and stone portions of the pallasites are given. In the case of the latter, the higher helium content of the stone portion is at least partly due to the higher radium content, but it has also been suggested that the iron has entered the stone matrix at some later date. This can be determined when the radium contents are known.

TABLE 6

The ages of the meteorites

NAME	He × 10^6	Ra × 10^{14}	AGE IN MILLIONS OF YEARS
	cc. per gram	*grams per gram*	
Savik	< 0.0002	—	
Toluca	1.2	21	16
Seeläsgen	2	—	
São Julião	2	—	
Mount Joy	9.7	4.7	570
Cocke County	14	4.0	930
Nelson County	20	1.8	2600

The question of the origin of the meteorites, whether from our own planetary system or from interstellar space, has been fully discussed by Paneth in a lecture to the Bunsen Gesellschaft (24) in the light of these results. If we accept the long period for the universe, the age of our solar system is most probably only of the order of one-thousandth of the age of the universe or on the short period estimate about one-third. If only some of the meteorites

TABLE 7*

The age of the meteorites

NAME	He × 10^6	Ra × 10^{14}	AGE IN MILLIONS OF YEARS
	cc. per gram	grams per gram	
Savik (Cape York)	< 0.0002	< 0.2	—
Coahuila	0.23	—	—
Uwet	0.39	—	—
Bethany, Farm Goamus	0.48		
	0.42	1.3	100
Bethany, Farm Gröndorn	0.49	—	—
Löwenfluss	0.47	—	—
Braunau	0.53	—	—
Canon Diablo	1.05	—	—
Magura	1.19	—	—
San Martin, Chile	2.13	1.4	420
Copiapo	2.51	—	—
Santa Rosa, Colombia	3.14	—	—
Nejed	3.7	—	—
Tamarugal	4	2 0	550
Seelasgen	4.87	4.9	120
Cranbourne	4.96	0.8	1600
Augustinowka	5.21	—	—
Toluca	5.82	17.0	100
Arispe	7.22	1.3	1500
Mooranoppin	7.54	—	—
Narraburra Creek	11.44	—	—
Wichita County	11.50	1.3	2100
San Angelo	11.86	4.2	800
N'Goureyma	13.91	2.9	1250
Hraschina	14.9	2.6	1450
Sacramento Mts	15.03	2.5	1550
Seneca Falls	15.03	2.0	1900
Charcas	15.65	4.4	1000
Silver Crown	17.35	—	—
Staunton, Mass. III	18.82	2.1	2150
Staunton, Mass. V	18.92	2.4	2000
Joe Wright Mt	19.28	4.1	1200
Burlington	19.31	3.6	1400
Williamstown	20.77	2.1	2400
Lenarto	22.23	2.3	2300
Carthage	23.84	—	—
Thunda	28.57	2.3	2800
Mount Ayliff, South Africa	35.81	2.8	2800

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* In all the determinations the helium and radium were measured in the same sample.

have an interstellar origin, we might expect to find some of an age older than that of the solar system. The ages given in tables 6 and 7 are maxima, but as may be seen from table 5 they would be reduced by only about 15 per cent, taking into account thorium in the ratio Th/U = 1.0, which according to V. M. Goldschmidt is the upper limit of the thorium content of such material. However, even neglecting this correction, the oldest found meteorites are not over the possible border line of the time of formation of the solar system. Taking into consideration the thorium, the ages of some meteorites are still greater than the oldest known minerals estimated by the lead method.

TABLE 8

The helium contents of various portions of the meteorites

NAME	ACCESSORY PORTION		IRON PORTION
	Description	He × 10^6	He × 10^6
		cc. per gram	*cc. per gram*
Magura	Troilite	0.13	1.19
	(Sulfide)	0 09	
Seeläsgen	Troilite	2.73	4.87
		2	
Cranbourne	Troilite	3.13	4.96
		1.40	
Wichita County	Troilite	9.07	11.50
Santa Luzia	Rind (Oxide)	1.06	—
	Schreibersite (Phosphide)	1.25	—
Brenham (Pallasite)	Stone	6.36	
	(Olivine)	6.87	1.11
Krasnojarsk (Pallasite)	Stone weathered away	—	1.21
Mincy (Pallasite)	Stone	21.7	4.81

The age of the substance of the earth

As has previously been mentioned, following the success of the preliminary investigation of the meteorites, Holmes and Dubey attacked the problem of the estimation of geological age by the helium method. Their results have already been given in table 3. Tables 3, 6, and 7 probably contain all the present available modern determinations, but the results of the prolonged studies of Strutt (Lord Rayleigh) already referred to should not be omitted from consideration in this problem. Space does not permit the inclusion of his results, which have conveniently been tabulated in the two books of previous reference (9). The author, in collaboration with Professors A. C. Lane and F. Paneth, has under completion a study of the ages of a comprehensive series of the Keweenawan rocks and minerals. The helium content of these fine-grained basalts was found to vary between 195×10^{-6} and 14.5×10^{-6} cc. per gram, but the copper minerals were found to contain much less, the lowest being 0.17×10^{-6}. The native copper contained in 32 grams between 10^{-9} and 10^{-10} cc. of helium. This infers from an approximate knowledge of the age that the radium content of the copper would be too small to detect, as was actually the case. The radium contents of the Keweenawan rocks have been published (42), but the ages cannot be given until the thorium contents have been accurately measured.

CONCLUSION

There thus remains open a very wide field of research on the rocks, one of the most prolific materials of the earth's crust, the results of which will be of great interest in the building up of a closely graded geological time scale, but the applications are not limited to the geological field; nature has supplied us a source of cosmic material in the form of meteorites to aid our probe, at least, into interplanetary space.

APPENDIX I

The age of a radioactive mineral is given by a knowledge of the ratio $\frac{\text{Original uranium}}{\text{Present uranium}}$. If the crystal network has remained unchanged, and there is evidence of such in at least one uraninite, then, as A. C. Lane has suggested, the total oxygen associated with the uranium and lead present in the uraninite today is to the original uranium as the ratio of oxygen to uranium in UO_2. This oxygen is distributed at present in the forms UO_2, UO_3, and PbO. In analysis reports the oxygen of the lead monoxide is usually counted twice, and thus to find the oxygen associated with the original uranium as UO_2, one calculates the oxygen of the present day $UO_2 + UO_3$ found by analysis. Having determined this quantity, the amount of original uranium is calculated from the formula UO_2. The present uranium is known by analysis and hence the age can be determined. The Wilberforce uraninite referred to above is the only material on which the fivefold check of the age has so far been applied. The results are shortly to be published by A. C. Lane.

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RAMAN SPECTRA IN INORGANIC CHEMISTRY

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I. INTRODUCTION

There are few physical discoveries which have resulted in a greater stimulation to investigations in a particular field than the discovery of the Raman effect by Sir C. V. Raman in 1928. Since that time there have appeared more than a thousand publications, each of which has usually discussed the Raman effect in connection with different compounds. In reviewing the subject briefly it is necessary, therefore, to set some arbitrary limitations to the material to be covered. Except in specific cases, discussions in this review will be limited to the more or less characteristic developments since 1930, it being assumed that the references and data given in Kohlrausch's "Der Smekal-Raman Effekt" (3) and the summaries by Ganesan (2) and Bhagavantam (1) will cover the material prior to that time, while the bibliography by Sirkar (6) will be supplementary.

Other arbitrary distinctions may be made, namely, theoretical aspects of the Raman effect, physical aspects, and empirical investigations. The first of these is considered to deal with the more strictly spectroscopic applications of the Raman effect, that is, the information which may be gained in regard to the various energy levels of a molecule.

So far as these applications are concerned, they are naturally intimately connected with band spectroscopy, which has been discussed in detail by Mulliken (4, 5) and by Villars (7) in This Journal. Raman spectra, however, are concerned with a more limited field, dealing mainly only with the vibrational and rotational transitions of a given system and rarely, if ever, with electronic transitions. The selection rules governing these transitions, however, are not identical with those governing infra-red absorption, which is likewise chiefly concerned with vibrational and rotational transitions, so that corollary information of value is obtainable from the Raman effect. Furthermore, because of their comparative simplicity and the relative strength of fundamental vibrations as compared to harmonics, Raman spectra are interpreted much more easily than infra-red or visible band spectra.

In the physical applications there might be classed the information that Raman spectra give as to spacial distributions of atoms and molecules, specific heats, electric moments, Boltzman distributions, and other more strictly physical properties.

Empirical investigations may be classified in two parts—organic and inorganic chemistry—with, however, the usual overlapping between these two subdivisions. For the purpose of this review the inorganic subject matter will be dealt with first and the organic reserved for later publication. The same principles apply to both fields of investigation, in particular the extrapolation of logical conclusions from one field to the other. Nevertheless, there is sufficient demarcation between these two general subdivisions of chemistry to warrant their separate treatment, both from the point of view of the material to be covered and because of a somewhat different emphasis in the two lines of investigation.

Empirical observations deal with the observed values of Raman lines (often referred to as modified lines, Raman shifts, frequency displacements, and Raman rays). These have yielded many interesting and fruitful results pertaining to the constitution of organic compounds and inorganic compounds in solutions, vapors, solids, and liquids, and have a much wider application than is obtainable from strictly theoretical considerations. From the latter point of view, alone, Raman spectra suffer equally with band spectra, quantum mechanics, and, to a certain extent, infrared absorption spectra, the limitations imposed by being practically applicable only to relatively simple molecules according to chemical concepts.

While susceptible to modification on the basis of accumulation of new data, these empirical observations, however, are now based on a sufficiently large number of statistical observations to contain more than an element of truth and to carry the same weight as any experimentally determined fact. Their interpretation is, however, a matter of opinion and can be viewed as correct only in the degree of reasonableness by which it explains known facts. This type of observation has, in the main, been extremely consistent with known chemical and physical behavior. There are, however, many interesting cases where the Raman results have been either divergent or applicable where no other method will yield results.

This procedure is particularly advantageous in the case of solutions, about whose complexity little is known, in the study of polymers and of amorphous solids, and in the chemical constitution of organic and inorganic compounds whose structure is open to question. It is for this reason that the discussion of empirical observations will be given the greatest weight in this summary.

DEFINITION OF TERMS

The most commonly used method of expressing Raman shifts is in terms of wave numbers or the number of vibrations per centimeter. Since the Raman lines are generally regarded as frequency differences, it is more or less customary to employ $\Delta\bar{\nu}$ to express this. The actual frequency (vibrations per second) of any Raman line is given by the expression $\nu\lambda = 3 \times 10^{18}$, where the digits represent the velocity of light in Ångström units (Å. or A. U.), and λ is the wave length, also expressed in Ångström units. In wave numbers per centimeter (number of waves per centimeter) this becomes

$$\frac{10^8}{\lambda_{(A.U.)}}$$

where $\bar{\nu} = \nu/c$. The term c is the velocity of light in centimeters per second (3×10^{10}). $\Delta\bar{\nu}$ is obtained from the following:

$$\bar{\nu}_1 - \bar{\nu}_2 = \pm \Delta\bar{\nu}$$

where $\bar{\nu}_1$ are the wave numbers per centimeter of the exciting radiation and $\bar{\nu}_2$ the wave numbers per centimeter of the Raman radiation.

In the case of frequencies as calculated from *mechanical* models, expressed in terms of wave numbers per centimeter, these are sometimes given as $\bar{\nu}$, since this term in these models represents an actual frequency and not a frequency difference. The numerical value of $\bar{\nu}$ thus calculated is theoretically equivalent to $\Delta\bar{\nu}$ obtained from spectroscopic data. However, for the sake of convenience in deriving the frequency terms arising from different molecular configurations, the letter n will frequently be used in place of $\bar{\nu}$. (See equation 4, for example.) It is related to $\bar{\nu}$ by the following equation:

$$n^2 = 5.87 \times 10^{-2} \cdot \bar{\nu}^2$$

Experimentally observed Raman shifts will be given in wave numbers per centimeter, as for example, $\Delta\bar{\nu} = 296$ cm.$^{-1}$, or, more simply, $\Delta\bar{\nu}$ 296. In particular instances it may also be of advantage to express the Raman shifts in terms of the corresponding wave length in the infra-red. This is related to $\Delta\bar{\nu}$ (in cm.$^{-1}$) by the following expression:

$$\Delta\bar{\nu} = \frac{10^4}{\lambda_\mu}$$

where lambda (λ) is expressed in μ or 10^{-4} cm.

The exciting radiation giving rise to the Raman lines will be expressed in round numbers in terms of Ångström units. It is usually impossible to say whether any of the recorded values of Raman shifts are corrected to vacuum or not.

Other terms employed are $\bar{\mu}$, representing the reduced mass, that is

$$1/\bar{\mu} = 1/m_1 + 1/m_2$$

where m_1 and m_2, etc., are the atomic weights of the vibrating masses in a mechanical system. This may also be written

$$\frac{1}{\mu} = \frac{1}{M} + \frac{1}{m}$$

where M and m have the same significance as m_1 and m_2. Further, for the sake of convenience the relation $(M + 2m)/m$ may be abbreviated as p.

F is the elastic restoring force or the force per unit displacement expressed in dynes per centimeter.
d is the deformation force constant in dynes per centimeter.
h is Planck's constant, 6.54×10^{-27} erg seconds.
N is Avogadro's number, 6.06×10^{23}.
ρ is the degree of depolarization.
k is the Boltzmann constant, 1.37×10^{-16} erg per degree.

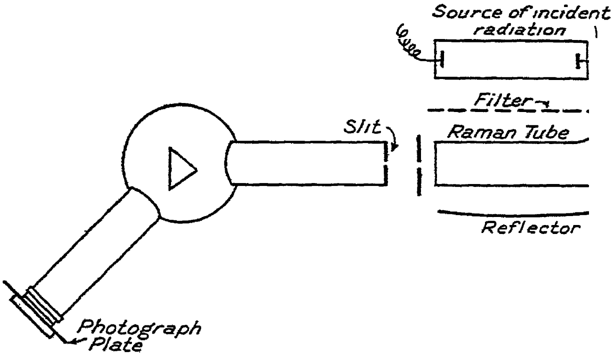

FIG. 1. SCHEMATIC DIAGRAM OF RAMAN APPARATUS
Showing spectrograph, Raman cell, exciting source, reflectors, and filters

II. THEORY

A. THE ORIGIN AND MAGNITUDE OF RAMAN FREQUENCY SHIFTS

The first approach to this subject is to discuss the method employed to produce the Raman effect. Essentially the method is to irradiate the substance to be examined with radiation as nearly monochromatic as possible. The material traversed by the light beam becomes a seat of emission, particularly observable in a direction normal to the incident beam. This light emerges at right angles to the incident radiation, enters the slit in the spectrograph, and is registered on a photographic plate. This arrangement is depicted schematically in figure 1. This emergent or "scattered" light may owe its origin to several causes, namely, "Rayleigh" scattering from particles of colloidal size and molecules themselves, if the material is homogeneous, direct reflection if it is inhomogeneous, fluorescent emission if fluorescence is possible, and true Raman scattering. Frequently all of these factors are simultaneously operative.

The principal emissions are due to Rayleigh scattering and reflection. These result, however, in no alteration of the incident spectrum, and the lines thus recorded are merely those belonging to the incident radiation. Fluorescence and Raman spectra are secondary effects and result in the emission of light different from that to which they owe their origin, a phenomenon which has long been known in the domain of x-rays (Compton effect).

In the optical phenomenon known as the Raman effect, the quantum of light colliding with the molecule of the irradiated material is debased, that is, it loses some of its energy to the molecule in the same fashion as any inelastic collision involving a quantum process.

This energy is absorbed as increased vibrational and rotational energy, and the resultant light scattered or emitted is *usually* of greater wave length than the impinging light by a definite amount, according to the quantum process involved. However, if the molecule is in a higher energy state than its normal state, the emitted light *may* have greater frequency or shorter wave length than that of the exciting source, resulting in what are sometimes called "anti-Stokes" lines. In either case the lines which thus appear are not present in the original radiation and are a function of the molecular constitution of the irradiated substance.

This conception of an interaction of a light quantum and a molecule to produce modified radiation is not new. It was postulated by Smekal (67) and is embraced by the Kramers-Heisenberg dispersion theory (35). Experimentally, however, such observations were first made by Raman (55), and treated shortly thereafter by Cabannes (19), Landsberg and Mandelstam (37, 38), and Rocard (59). The next consideration is the relation between absorption and emission in these processes.

Infra-red absorption and the Raman effect

The above conception of photon collision may be arithmetically represented as follows:

If E_l and E_k represent two energy levels of a molecule, the frequency $\nu_{l,k}$ given by the quantity $(E_l - E_k)/h$ may manifest itself in a scattered spectrum giving rise to various Raman lines represented by $\nu_0 \pm \nu_{l,k}$, where ν_0 is the frequency of the incident quantum of radiation.

Actually, however, there are certain limiting conditions: Raman lines do not always correspond to infra-red absorption bands, as this would indicate. It has been pointed out by Langer (40, 41) and by Dieke (27) that it is necessary to start with molecules not in a single "eigen" state but with the system capable of being excited in two of its characteristic states represented by l and k, and that transitions should be possible for the molecules from either of these states to a third energy level represented by n. It is immaterial whether the transitions from l to k are forbidden or not. If the transition $\nu_{l,k}$ is forbidden, there would be no absorption corresponding to this frequency, whereas if a third discrete level n exists to which transitions from l and k may take place, the same $\nu_{l,k}$ would give rise to a Raman line. On the other hand, if no n (common third level) exists, an absorption line would be present corresponding to $\nu_{l,k}$, but not a Raman line. This may be also expressed as

$$A_{kn}A_{kl}\left[\frac{1}{\nu_{kn} \pm \nu_0} + \frac{1}{\nu_{ln} \pm \nu_0}\right](\nu_{kl} \pm \nu_0)^2 \qquad (1)$$

where A_{kn} is a matrix element for $\int r\, \psi_k \psi_n\, dx$, which describes the intensity of the transition between the states k and n giving out radiation

$$\nu_{kn} = \nu_k - \nu_n = \frac{E_k - E_n}{h} \qquad (2)$$

The modified frequencies $\nu_{kl} \pm \nu_0$ differ from the incident frequency ν_0 not by an absolute amount but by differences between these; that is, only when two allowable transitions A_{kn} and A_{ln} (different from zero) have a common level n is there any intensity in the scattered frequency.

The Raman shifts as compared with the infra-red absorption in carbon tetrachloride are indicated in figure 2, where the vertical dotted lines represent the Raman transitions and the vertical solid lines the infra-red absorption. This is somewhat idealized. It may be pointed out that while a non-concordance of a few wave numbers between infra-red absorption and Raman spectrum lines may have vital significance to a physicist, a small difference is of little moment to the chemist from the point of view of identification of a given transition for analytical purposes.

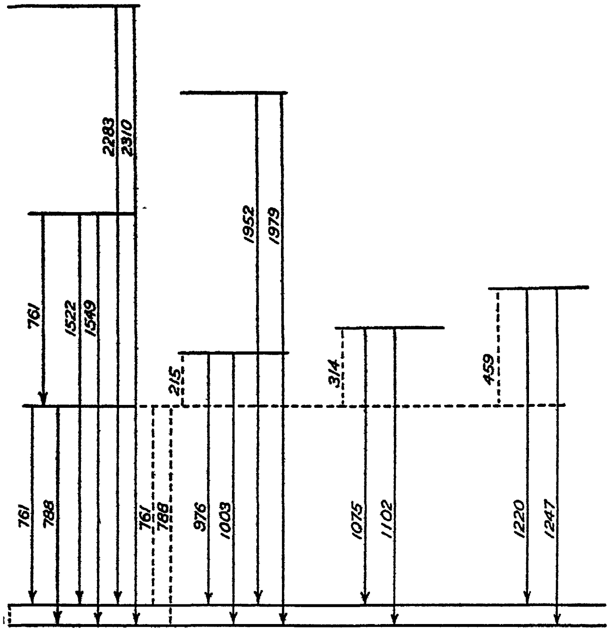

FIG. 2. TRANSITIONS GIVING RISE TO RAMAN LINES AND INFRA-RED ABSORPTION

The vertical dotted lines represent the possible Raman lines. The corresponding $\Delta\bar{\nu}$ are indicated numerically (after Langer).

In the case of simple molecules it is possible to state *a priori* which frequencies would appear as Raman lines and which as absorption lines, and which others may appear as both, as has been demonstrated by Rasetti (58). The intensity of the Raman emission is dependent in part on the symmetry character of the initial and final states and on the classical electric moment. Symmetrical oscillations cannot affect the electric moment and the frequency is therefore termed *"inactive,"* and cannot appear, except in combination, associated with an unsymmetrical vibration or *"active"* frequency. (These are also termed optically active and inactive.) Since the Raman lines depend for their intensity on the electric moments of interaction with intermediate states, the inactive frequencies are especially favored. Van Vleck (70) considers that the most intense Raman lines are those whose displacements are equal to one of the fundamental frequencies and, second, the Raman lines whose shifts are the harmonics of a fundamental or are combination frequencies. The most intense scattering, however, is the ordinary Rayleigh scattering.

Raman spectra and selection rules

It has already been mentioned that the great majority of molecules are in their normal vibrational states and that transitions, therefore, are mostly characterized by their change from $0 \rightarrow 1$ vibrational quantum numbers. Similarly, Raman spectra may also indicate rotational and rotational-vibrational transitions.

The selection rules in the Raman effect have been determined by Rasetti (58). A discussion of these rules is, in part, a recapitulation of some of the material already mentioned. In order that a shift corresponding to the transition $l \rightarrow k$ may be observed, it is necessary that both states l and k combine at least with a third state n, the Raman spectrum becoming particularly intense when the energy $h\nu_0$ of the impinging quantum is near to $E_n - E_l$. If $E_n - E_l$ equals $h\nu_0$ we have fluorescence instead of the Raman effect.

In the case of a linear molecule in the lowest electronic state and in the Jth rotational state ($J = 1, 3, 5$, ---), it can be said that this state combines only with the $J - 1$ and $J + 1$ rotational states of the upper electronic level. The first of these combines with the J and the $J - 2$ rotational states of the normal electronic level and the second with the J and $J + 2$. So, on the whole, the possible Raman transitions from the J rotational states to other rotational states are $J \rightarrow J - 2$, $J \rightarrow J$, and $J \rightarrow J + 2$. The second term involves no energy change, that is, gives scattered light of unmodified frequency. The transition involving a degradation of frequency is the $J \rightarrow J + 2$, the remainder giving anti-Stokes lines symmetrical with respect to the exciting lines. Applications of this conclusion will be discussed later in the Raman effect of gases.

Raman effect and molecular configuration

Correlation of the natural frequencies of vibration with molecular structure can be effected by the investigation of the characteristic modes of oscillations of simple polyatomic molecules. This has been done by Dennison (25, 26) for such molecules as carbon dioxide, ammonia, and methane. Bhagavantam (14), from the point of view of Raman spectra, has recalculated the available data for simple molecules of the types X_2, X_3, X_4, AX_2, AX_3, and AX_4, with the assumption that the fields of force are centered around each nucleus, that the displacement of individual particles from their mean position is infinitesimal, that one is concerned only about oscillations around an equilibrium configuration, and that the symmetries of the electron configuration remain essentially undisturbed at the instant of each displacement.

Other calculations have been made by Bates and Andrews (13), Yates (76, 77), Andrews (8, 9, 10, 11), Salant (60, 61), Ellis (29), Kohlrausch (3), Lechner (42), Radakovic (57), and Lespieau, Bourguel, and Wakeman (43).

The theory of force systems of three or more mass particles can be considered only an approximation. Notwithstanding this, however, the application of equations derived from simple systems to more complicated ones has in some cases led to interesting conclusions. That specific quasi-harmonic oscillations exist in complicated molecules has been convincingly demonstrated by dynamic properties of mechanical models (31). Of the several concepts of force systems between mass particles, that of directed bond forces has yielded the most fruitful results. This was postulated by Andrews (8) on the basis of specific heat values, and it was subsequently pointed out by him (10, 11) that Raman spectra confirmed this hypothesis. This was the first attempt to correlate Raman spectra with molecular vibrations and to indicate that the Raman shifts really gave fundamental natural frequencies.

(*a*) *Diatomic molecules.* The simplest type of oscillator is one with a single fundamental frequency, such as oxygen, for example ($\Delta\bar{\nu}$ 1555), or chlorine ($\Delta\bar{\nu}$ 556). With molecules of the type of X_2 one can assume a dumb-bell type of molecule, in which the two atoms are held together with a force (F) which may be expressed in dynes per centimeter. If the force is large, the characteristic frequency of vibration will be rapid. If the two atoms are heavy, the characteristic frequency will be slow. From the equation for a simple harmonic oscillator in a mechanical system, one obtains the following relationship:

$$\nu = \frac{1}{2\pi} \cdot \sqrt{F/m} \tag{3}$$

where ν represents the frequency of vibration per second, m the mass of the vibrating components, and F the force exerted between them. In an atomic system, if ν is expressed in wave numbers per centimeter and masses by relative atomic weights, this may be written:

$$\frac{\sqrt{N}}{2\pi c}\sqrt{\frac{F}{\bar{\mu}}} = 4.125\sqrt{\frac{F}{\bar{\mu}}} \quad \text{or} \quad n = \frac{\bar{\nu}}{4.125} = \sqrt{\frac{F}{\bar{\mu}}} \tag{4}$$

where N is Avogadro's number and c the velocity of light, $\bar{\mu}$ the reduced mass and $n^2 = 5.87 \times 10^{-2} \cdot \bar{\nu}^2$.

To calculate F, this reduces to

$$F = \nu^2\left(\frac{4\pi^2c^2}{N}\right)\bar{\mu} \text{ (dynes per centimeter)} = 5.87 \times 10^{-2} \cdot \bar{\nu}^2\,\bar{\mu} = n^2\,\bar{\nu}^2\,\bar{\mu} \tag{5}$$

If F is the restoring force in the system and the greatest amplitude of vibration is $\bar{a}$, the mean restoring force is $1/2\bar{a}^2F$, which may be equated to $h\bar{\nu}c$, hence or

$$\bar{a} = 8.2 \times 10^{-8} \sqrt{\frac{1}{\bar{\mu}\bar{\nu}}}\ \text{cm.} \tag{6}$$

In the diatomic oscillator, therefore, if one can determine the frequency of oscillation, then the amplitude of vibration and force constant are also calculable. These are only fairly approximate. Nevertheless, from the characteristic frequencies of "inner" vibrations, that is, the oscillations between two given atoms in a molecule (even though that molecule may not be merely a diatomic one), it has been possible to calculate the approximate relative binding force. The amplitude of vibration calculated by this method varies from 0.06 to 0.09 A. U.

(b) *Polyatomic molecules* (1). In general, for more complicated systems Radakovic (56) and Kohlrausch (32) have shown that if the mechanical frequency $\bar{\nu}$ be expressed in wave numbers per centimeter, and the mass in relative atomic weights, and if $n^2 = 5.87 \times 10^{-2} \cdot \bar{\nu}^2$ (cf. equation 5) is introduced as an abbreviation, then the characteristic determinant whose roots give the normal vibrations is for the general case

$$n^6 - an^4 + bn^2 - \bar{c} = 0 \tag{7}$$

$$a \equiv n_1^2 + n_2^2 + n_3^2 = \frac{F_0}{\bar{\mu}_0} + \frac{F_1}{\bar{\mu}_1} + \frac{F_2}{\bar{\mu}_2}$$

$$b \equiv n_1^2 n_2^2 + n_1^2 n_3^2 + n_2^2 n_3^2 = \frac{F_0 F_1}{\bar{\mu}_0 \bar{\mu}_1} + \frac{F_1 F_2}{\bar{\mu}_1 \bar{\mu}_2} + \frac{F_0 F_2}{\bar{\mu}_0 \bar{\mu}_2} - \frac{F_0 F_2}{m_0^2} \cos^2 \alpha_0 - \frac{F_1 F_0}{m_1^2} \cos^2 \alpha_1 - \frac{F_2 F_1}{m_2^2} \cos^2 \alpha_2 \tag{8}$$

$$\bar{c} \equiv n_1^2 n_2^2 n_3^2 = F_0 F_1 F_2 \left[\frac{1}{\bar{\mu}_0 \bar{\mu}_1 \bar{\mu}_2} - \frac{\cos^2 \alpha_2}{m_2^2 \bar{\mu}_0} - \frac{\cos^2 \alpha_1}{m_1^2 \bar{\mu}_2} - \frac{\cos^2 \alpha_0}{m_0^2 \bar{\mu}_1} + \frac{2 \cos \alpha_0 \cos \alpha_1 \cos \alpha_2}{m_0 m_1 m_2} \right]$$

where m_0, m_1, and m_2 are the relative masses, and F_0, F_1, and F_2 the binding forces and α_0, α_1, and α_2 the valence angles as indicated in figure 3.

The general case described in equation 7 cannot be immediately applied. However, in simplified cases with molecules of more or less high degree of symmetry a practical application may be made.

(2) Triatomic molecules. With molecules of type AX_2 there are

two possibilities: if the molecule is linear there exist a symmetrical oscillation, as shown in II (A, figure 4), an asymmetric oscillation, as shown in I, and a deformation oscillation, as shown in III. If the molecule is non-linear, of type AX_2, the oscillations are indicated by B. This leads to three equations relating the mechanical frequencies to the restoring force and the respective masses for the linear model:

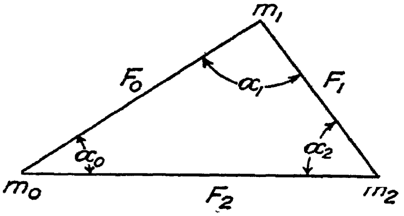

FIG. 3. DISTRIBUTION OF FORCES AND MASSES IN A POLYATOMIC MOLECULE

The masses are represented by m, the interatomic forces by F, and the valence angles by α

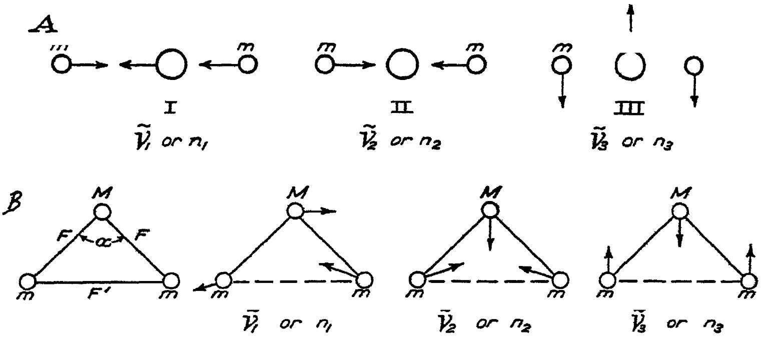

FIG. 4. POSSIBLE TYPES OF OSCILLATION IN LINEAR AND NON-LINEAR MOLECULES OF TYPE AX_2

A represents the type of motion in a linear model and B the motion in a non-linear model.

$$n_2 \qquad\qquad (a)$$

$$n_1 = \sqrt{F \times \frac{M + 2m}{Mm}} \quad (b) \qquad\qquad (9)$$

$$n_3 = \sqrt{\qquad \frac{M + 2m}{}} \quad (c)$$

Hence the ratio of n_1 and n_2 is given by

$$\sqrt{\frac{M + 2m}{M}} \tag{10}$$

We shall see presently how this relationship may fit specific examples. n_2 is a symmetrical vibration and will be the most intense.

In molecules of the type X_3 (which is a special case of type AX_2) spacially arranged in the form of an equilateral triangle and in which the masses and binding forces are equal, i.e., when

$$m_0 = m_1 = m_2 = m; \qquad F_0 = F_1 = F_2 = F; \qquad \alpha_0 = \alpha_1 = \alpha_2 = 60^\circ$$

then equation 8 reduces to

$$\left(n^2 - 3\frac{F}{m}\right)\left(n^2 - \frac{3F}{2m}\right)^2 = 0. \tag{11}$$

This gives two solutions according to Bhagavantam (14), namely,

$$n_1 = \sqrt{3\frac{F}{m}} \quad \text{and} \quad n_2 = \sqrt{3\frac{F}{2m}}$$

The latter value, being a double root, would split into two different frequencies by a disturbance of the symmetry. The ratio of the frequencies obtained is

$$\frac{n_1}{n_2} = \sqrt{2} \tag{12}$$

With molecules of the type AX_2 in which two light atoms are bound to the central atom with equal binding force, in the form of an isosceles triangle, the following relations are obtained, referring to B, figure 4, and comparing this with figure 3. Here one may consider

$$\begin{aligned} &m_0 = M && \alpha_0 = \alpha \\ &m_1 = m_2 = m && \alpha_1 = \alpha_2 = 90^\circ - \frac{\alpha}{2} \\ &F_0 = F_2 = F && p = \frac{M + 2m}{M} \\ &F_1 = F' && \end{aligned}$$

From the considerations of Dennison (26) and Bjerrum (17) the following three equations are obtained relating the frequencies of vibration with the valence angles and the respective masses:

$$n_1^2 = \frac{F}{m}\left[p + (1 - p)\cos^2\frac{\alpha}{2}\right] \tag{13a}$$

$$n_2^2 n_3^2 = 2\frac{F'}{m}\cdot\frac{F}{m}\left[p\cos^2\frac{\alpha}{2}\right] \tag{13b}$$

$$n_2^2 + n_3^2 = 2\frac{F'}{m} + \frac{F}{m}\left[1 - (1 - p)\cos^2\frac{\alpha}{2}\right] \tag{13c}$$

If there are no criteria for the magnitude of the valence angle, α, this can be approximated by comparing the experimental

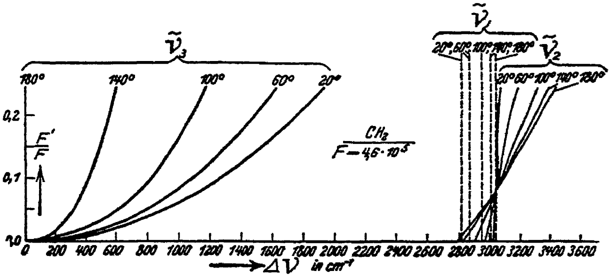

FIG. 5. POSSIBLE RAMAN FREQUENCY SHIFTS AS A FUNCTION OF VALENCE ANGLE AND RESTORING FORCES

(After Kohlrausch, "Der Smekal-Raman-Effekt")

frequencies with the three theoretical frequencies. The form of vibration belonging to n_1 must be so constituted that the distance from m to m is not altered by it. This vibration results in a displacement of the electrical center of gravity and is in consequence optically active. The relative vibrations as a function of the ratios of $F':F$ and the valence angles are given in figure 5.

Where Kohlrausch (33) gives these relations for the group CH^2, assuming a force constant of 4.6×10^5 dynes per centimeter, it is obvious, for example, that for $\alpha = 180°$, $\tilde{\nu}_3$ becomes 0, that $\tilde{\nu}_1$ is independent of $\frac{F'}{F}$ and increases with increased α, while $\tilde{\nu}_2$ decreases with increased α in cases of small values of $\frac{F'}{F}$.

In the case of the "valence force system," (34, 42, 57, 75), where the nature of F' is considered more in the light of a deformation force (d), n_1 is identical with equation 13a, but

$$n_2^2 n_3^2 = \frac{F}{m} \cdot \frac{d}{m} \cdot p$$

$$n_2^2 + n_3^2 = \frac{d}{m}\left[p + (1 - p)\cos^2\frac{\alpha}{2}\right] + \frac{F}{m}\left[1 - (1 - p)\cos^2\frac{\alpha}{2}\right] \qquad (14)$$

If the quantity $\dfrac{m^2}{M(M + 2m)}$ is small compared to 1,

$$n_1^2 = \frac{F}{m}\left[p + (1 - p)\cos^2\frac{\alpha}{2}\right];\ n_2^2 = \frac{F}{m}\left[1 - (1 - p)\cos^2\frac{\alpha}{2}\right];$$

$$\frac{d}{m}\left[p + (1 - p)\cos^2\frac{\alpha}{2}\right]. \qquad (15)$$

(3) Tetratomic and other molecules. For molecules of the type X_4, phosphorus, for example, Bhagavantam (14) deduces that the frequencies should be expressed by

$$n_1 = \sqrt{\frac{F}{m}}; \quad n_2 = \sqrt{\frac{2F}{m}}; \quad n_3 = \sqrt{\frac{4F}{m}} \qquad (16)$$

their ratio being $1:\sqrt{2}:2$. This assumes a tetrahedral model. For a quadrilateral model there are four independent modes of oscillation. For molecules of the type AX_3 there are four frequencies. The atoms in this model are at the apices of a pyramid, although in special cases the atom A may be in the plane of the X atoms. Molecules of the type AX_4 also have four normal frequencies and this model is likewise a tetrahedron. In the vibration associated with n_1, it is supposed that the tetrahedron expands or contracts symmetrically, the central atom remaining fixed at the center of gravity. The third frequency is attributed to the motion of the central atom vibrating about its mean position within the tetrahedron.

(4) Summary. The foregoing discussion has summarized the treatment of simple molecular configurations and the atomic oscillations as a mechanical problem. This has been based on the

"central force system," "valence force system," and Dennison's system, the essential difference between them being the directions in which the forces act and the magnitude of the forces in the equilibrium state. In complicated molecules, the complete quantitative determination of the mechanical vibration frequencies (and consequently the vibrational Raman spectra which would correspond to these oscillations) is practically an impossibility. Nevertheless, qualitative information as to the mode of possible vibrations, and the molecular configuration to which these owe their origin, is of a distinct utility in the allocation of different Raman lines. Furthermore, as a first approximation, a fairly complicated molecule can be considered as made up of *group units*, and the binding force determined from relatively simple equations. The equations particularly applicable to the elucidation of structural relationships, given herein, are equations 4, 9, 10, 12, 15, and 16.

For the sake of clarity, specific examples may be mentioned: The three observed Raman frequencies for carbon dioxide expected for a linear model are $\Delta\bar{\nu}$ 2350, 1330, and 680; for carbon disulfide, $\Delta\bar{\nu}$ 1470, 655, and 745, corresponding to $\Delta\bar{\nu}_1$, $\Delta\bar{\nu}_2$, and $\Delta\bar{\nu}_3$, respectively. According to equation 10,

$$\frac{\Delta\bar{\nu}_1}{\Delta\bar{\nu}_2} = \sqrt{\frac{M + 2m}{M}}$$

or, for example, with carbon dioxide,

$$1.77 = \frac{2350}{1330} \cong \sqrt{\frac{12 + 32}{12}} = 1.91$$

Or for carbon dioxide the ratio $\frac{\Delta\bar{\nu}_1}{\Delta\bar{\nu}_2}$ observed is 1.77; calculated from equation 10, 1.91. For carbon disulfide this is 2.24 (observed) and 2.51 (calculated).

Applying equation 4 to group oscillations of a series of alcohols, Trumpy (69) obtained the following:

	$\Delta\bar{\nu}$ *Observed*	$\Delta\bar{\nu}$ *Calculated*
(CH_3)—(OH)	1040	1055
(C_2H_5)—(OH)	890	910
(C_3H_7)—(OH)	857	855
(C_4H_9)—(OH)	823	823

Calculations of the valence angle, α, in non-linear simple triatomic molecules can be made approximately from the following:

$$\frac{n_1}{n_2} = \sqrt{\frac{M + 2m \sin^2 \alpha}{M + 2m \cos^2 \alpha}} \tag{17}$$

which is based on previously given considerations. This leads to the following values of α for the compounds listed:

	α
$O{=}C{=}O$	180°
$S{=}C{=}S$	180°
$H{-}S{-}H$	90°
$O{=}S{=}O$	120°

The application of equation 4 to calculate the binding force to specific types of chemical linkage is obtained from the Raman spectra examination of simple substances which contain either this linkage alone, as in the case of diatomic molecules, or by attributing a specific Raman frequency to a type of binding by empirical but nevertheless logical means. This is accomplished in the following manner: In figure 6 are given the Raman frequency shifts for several organic compounds.

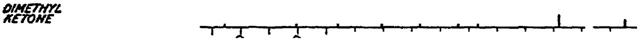

FIG. 6. CHARACTERISTIC RAMAN FREQUENCY SHIFTS AS A FUNCTION OF CHEMICAL CONSTITUTION

It is apparent in the case of methane that the only linear harmonic oscillation possible is that of hydrogen against carbon (the two highest-frequency weak lines are doubtful). The shift at $\Delta\bar{\nu}$ 2915 is therefore attributed to the carbon–hydrogen oscillation. This is substantiated by the fact that carbon tetrachloride, which contains no hydrogen, has no Raman shifts in this region. In the case of ethane, where there is both a possibility of carbon-to-carbon and carbon-to-hydrogen oscillations, the appearance of a line at $\Delta\bar{\nu}$ 999 is obviously indicative of the carbon-to-carbon oscillation. This does not *a priori* exclude $\Delta\bar{\nu}$ 1460, but from other considerations which will not be discussed at this time, $\Delta\bar{\nu}$ 1460 has been found to be due to the deformation oscillation of the H—C linkage. Ethane has more than one linear harmonic carbon-to-hydrogen oscillation. In the case of the acid and the ketone the $\Delta\bar{\nu}$ 1647 and 1712, respectively, are correctly attributable to C=O, since these lines only appear in this region in compounds containing such linkages. From these and similar considerations with other compounds, both organic and inorganic, one is able to estimate the restoring force exerted by the atoms in the normal state. In the case of questions of disputed structures, a more careful analysis is necessary, and the identification of other frequency lines corresponding to the probable oscillation frequencies of a given molecular configuration is essential. In table 1 are given some types of atomic linkages and their corresponding restoring forces.

TABLE 1

Valence forces (F)

LINKAGE	$F \times 10^{-5}$ DYNES CM.$^{-1}$	LINKAGE	$F \times 10^{-5}$ DYNES CM.$^{-1}$
C—H	5.02	C—C	4.40
N—H	6.39	C—N	4.53
O—H	6.72	C—O	5.05
Cl—H	4.38	H—H	5.38
C=C	11.0	C≡C	14.82
C=O	11.7	C≡N	19.23
O=O	11.4	C≡O	18.83
		N≡N	22.30

This leads to the conclusion that the binding force between the atoms executing a simple harmonic displacement from an equilibrium position does not depart far from 5×10^{-5} dynes per centimeter as an average value for a single linkage. The departures from this average, however, have significance. It is also equally clear that atoms joined with a double bond are held together with valence forces approximately twice as great as in the case of the single bond. In the case of triple bonds, the forces exerted by the similar atoms are approximately three times those of the same atoms joined with a single bond. In some cases this force constant is greater than three times the constant for a single bond. This evidence from Raman spectra has, for instance, long indicated the nature of the triply bonded oxygen to carbon in carbon monoxide, a conclusion to which Langmuir came from chemical considerations more than a decade ago, and to which Pauling (53) has recently come from quantum-mechanical considerations.

B. INTENSITIES OF RAMAN LINES

Raman frequency shifts may be completely described only in terms of three coördinates, namely, magnitude of the shifts, their intensities, and their degrees of polarization. It has already been indicated that the magnitudes of the frequency shifts are primarily a function of the type of oscillation and are dependent, therefore, on the binding force and the relative mass of the oscillating components. From a general point of view the intensities of Raman spectra shifts are directly dependent upon the number of molecules present, which may act as emitters. This makes the Raman spectra studies of gases particularly difficult. Apart from this consideration, in general, the intensities of the Raman scattering follow approximately the same laws as are applicable to Rayleigh scattering, that is, they increase proportionately to λ^{-4}. This has recently been confirmed by Werth (74). Ornstein and Rekveld (49) compare the intensities of the Raman scattering from carbon tetrachloride, using mercury lines 5460, 4358, and 4047 A.U. as exciting lines. Similar observations were made with quartz (51). The Rayleigh fourth-power law was found to hold very accurately. This does not hold, however, when the frequency of the exciting line approaches the value

$$\frac{E_n - E_k}{h}$$

where E_n is the energy of the "third level" previously mentioned. Sirkar (63) observed that excitation by the 3132 A.U. mercury line results in Raman scattering about 1.38 times more intense than would be indicated by the Rayleigh fourth-power law relative to the 4358 line, and further (64) that the Raman lines of large frequency shifts deviate more from the fourth-power law than small shifts. He further postulates that large deviations may be due in part to changes in optical polarizability and anisotropy, these changes being quite different for different exciting lines and different modes of vibration (45, 46).

It has heretofore been pointed out that the relative intensities depend upon the nature and number of the "third levels" with which the initial and final ones in the Raman shifts can combine. The rules applicable to the relative intensities of individual Raman lines have been formulated by Van Vleck (70), the most intense scattering being from the symmetrical or inactive oscillations.

Relative Raman scatterings for individual compounds have been measured by Ellenberger (28), Segré (62), Landsberg and Mandelstam (39), and Weiler (72, 73). Intensities of specific Raman shifts will be further discussed in the consideration of individual compounds.

The vibrational anti-Stokes lines owe their origins to the fact that the molecules which act as their emitters are not in the normal vibrational state, but in a higher vibrational level. Since, at room temperature, the number of molecules in the higher vibrational states is usually small, the intensity of the anti-Stokes lines, as compared to the intensity of the normal shifts of reduced frequency, is usually very weak. Where they can be elicited, however, an estimation can be made of the population of the molecules in the higher vibrational states. Furthermore the increase in this population, as a function of temperature, may also be determined. From quantitative measurements of the relative intensities of the Stokes and anti-Stokes lines, it has been found that their ratio follows approximately as is to be expected from the Boltzmann distribution; that is,

$$n_{\nu_1} = \beta \cdot e^{\frac{-h\nu_1}{kT}}$$

where k is the Boltzmann constant, T the absolute temperature, and $h\nu_1$ the energy corresponding to the transition.

Ornstein and Rekveld (48, 50), Placzek (54), and Sirkar (65, 66), have suggested a modified formula. According to Sirkar, the ratio of the intensity of the Stokes and anti-Stokes lines is more accurately represented by the expression

$$\left(\frac{\nu + \nu_{mn}}{\nu - \nu_{mn}}\right)^4 \cdot e^{-\left(\frac{h\nu_{mn}}{kT}\right)}$$

(where ν is the incident frequency and $\nu \pm \nu_{mn}$ the modified radiation), as given by Placzek's theory than by the Boltzmann equation alone.

Actual experimental determinations of the relative intensities of the anti-Stokes and Stokes lines extend back as far as the measurements of Krishnan (36). Brickwedde and Peters (18) noted the rapid increase in the anti-Stokes line $\Delta\bar{\nu}$ 476 in quartz in going from −180° to 550°C. The anti-Stokes line $\Delta\bar{\nu}$ 124 increased less rapidly. The approximate validity of the Boltzmann equation has also been demonstrated by Daure (23). The increase in the intensity of the anti-Stokes lines for calcite with increase in temperature from 150° to 250°C. has been noted by Venkatesachar and Sibaiya (71). Quartz has been similarly examined between 18° and 500°C. by Ney (47), who also noted a slight decrease in the magnitude of the frequency shifts of the anti-Stokes lines, as well as their increased intensities.

C. DEPOLARIZATION OF RAMAN LINES

The degree of depolarization is the third coördinate necessary for a complete description of Raman emissions. It is well-known that general scattering of the Rayleigh type is more or less polarized when viewed in the direction normal to the incident radiation, the degree of polarization, however, depending somewhat on the anisotropic character of the molecule. The ratio of the intensity of the horizontal light vibration (i) to the vertical vibration (I) (which is generally preponderant) gives a measure of the degree of depolarization, that is, $\rho = \frac{i}{I}$ where ρ is the depolarization factor. In the phenomenon of diffusion from normal liquids, ρ can attain a value of 6/7.

The experimental studies of the polarization of Raman rays show that each ray can have a state of polarization independent of the normal diffused scattering and of other Raman rays simultaneously emitted. The value of ρ can vary between 0 and slightly less than 1 in liquids (24).

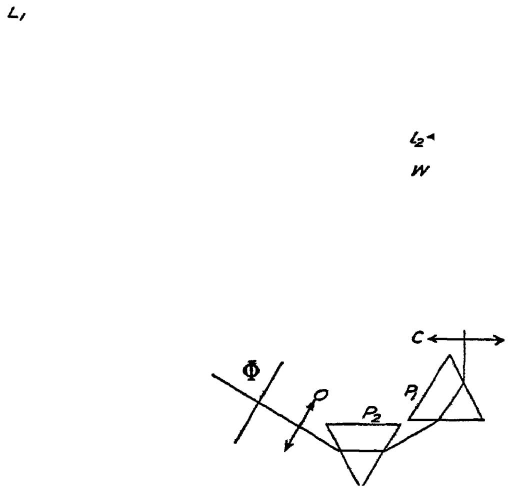

Fig. 7. Schematic Diagram of a Method Used to Determine the Degree of Depolarization of Raman Lines
(After Cabannes and Rousset)

Actual experimental measurements of the depolarization are exceedingly difficult, since the experimental arrangement requires the complete elimination of parasitic light. One of the most extensive series of such measurements has been carried out by Cabannes and Rousset (22). The experimental arrangement employed by them is given in figure 7. The image of the exciting source, S, is projected by the lens, L_1, on a point, A, in front of a rectangular aperture. The lens L_2 reprojects this image so that it is focused in the interior of the Raman tube, M. A third lens, L_3, serves a purpose analogous to periscopic collecting lenses. The Raman tube, M, is placed in a vessel containing a liquid having approximately the same index of refraction as the liquid to be studied. A planoconvex lens, of which the center of curvature is in M, is attached to the exit end of the Raman tube. A lens, l_1, projects the image of the interior of the tube, M, on a rectangular opening, B, and is thence reprojected on the spectroscopic slit, F. The ray diffused at right angles to the incident radiation consists of two incoherent rectangular vibrations, one of which is of maximum intensity, I, perpendicular to the incident ray, and the other is of minimum intensity, i, and parallel to the incident ray. To measure the depolarization factor, ρ, it is necessary to resolve the two diffuse beams. For this purpose a quartz prism, W, is placed before the slit, resulting in two spectral images, one above the other. A mica plate, m, is used to correct the unequal diminution of i and I in traversing the spectrograph prisms. The relative intensities of the two scattered beams may be determined microphotometrically or by other suitable means.

While other observers have used somewhat different experimental arrangements, they are in principle very similar. The description of this apparatus serves to clarify the picture. No brief description, however, can do justice to the care which must necessarily be exercised in carrying out these experiments. It will be pointed out later that some phases of development in Raman spectra depend on the development of the technique employed. In the case of depolarization measurements, this is an example *par excellence.*

According to Cabannes and Rousset, the Raman rays are the result of the interaction of the incident radiation and the fundamental frequency of atomic oscillation in the interior of a molecule. If the atomic nuclei were immovable in their position of stable equilibrium, the refractivity of the molecule and the diffusion of light would be completely defined by a symmetrical force constant (γ), but since this force varies, owing to the nuclei oscillating about their equilibrium positions, it is assumed that the force takes the value of γ_0. If the normal coördinate which defines the oscillation frequency n or $\bar{\nu}$ be designated by q, the

Raman rays $\tilde{\nu}_1 \pm \tilde{\nu}_2$ depend upon the derivative of the force $\left(\frac{\partial\gamma}{\partial q}\right)_0$, the same as Rayleigh scattering depends upon the force γ_0. The symmetrical force γ_0 is connected with two invariants a and b, which are called average refractivity and optical anisotropy. The depolarization factor of Rayleigh scattering by a perfect gas is given in terms of a and b, by the expression:

$$\frac{6b^2}{45a^2 + 7b^2} \tag{18}$$

The terms "average refractivity" and "optical anisotropy" can also be used in connection with the invariants relative to the force

$$\left(\frac{\partial\gamma}{\partial q}\right)_0$$

and the foregoing formula (equation 18) given for the depolarization factor applied to Raman radiation. There is, however, an essential difference between Rayleigh scattering of a perfect gas and Raman radiation. In the first case the three principal refractivities, of which a is the average, are all positive and the maximum value of ρ cannot exceed 1/2. In the second case the average refractivity can annul itself and ρ attains the value 6/7. The measurement of the depolarization factor in Raman rays permits an estimate of the symmetry and the configuration formed by the atomic nuclei in the interior of the molecule. The molecule in motion does not keep all the elements of symmetry of a molecule at rest, and the oscillations are inactive in *diffusion*, giving the Raman rays of which the depolarization factor is equal to 6/7; that is to say, the ray is depolarized. In order to solve the problem of molecular symmetry of the different possible models for a given molecule, it is necessary to determine *a priori* for each model the number of forbidden rays and the depolarized rays and to compare these results with the experimental determinations.

For example, in the case of sulfur dioxide three characteristic rays, $\Delta\tilde{\nu}$ 525, 1146, and 1340, are extant. The values of ρ found for these $\Delta\tilde{\nu}$ are, respectively, 0.6, 0.14, and 0.8. The strong ray, 1146, evidently corresponds to a symmetrical oscillation. There remains, then, the question of determining which of the rays $\Delta\bar{\nu}$ 525 and 1340 are provoked by asymmetric oscillation, that is, which gives a depolarization factor equal to 6/7. It is evident from the figures given above that $\Delta\bar{\nu}$ 1340 is the shift which corresponds to the asymmetric oscillation. There are two possibilities in interpreting these data, namely, $\Delta\bar{\nu}_1 = 1340$ and $\Delta\bar{\nu}_2 = 1146$, or $\Delta\bar{\nu}_1 = 1146$ and $\Delta\bar{\nu}_2 = 1340$. The first of these suppositions gives a valence angle for sulfur dioxide corresponding to 118°, the second an angle of 62°. It is evident from the measure of the depolarization that $\Delta\bar{\nu}_1$ is equal to 1340. Hence the calculation of the valence angle,

$$\cos \alpha = \frac{M + m}{m} \cdot \frac{\Delta\bar{\nu}_2^2 - \Delta\bar{\nu}_1^2}{\Delta\bar{\nu}_2^2 + \Delta\bar{\nu}_1^2}$$

gives a value of approximately 119°. In the case of compounds such as water, the most that can be said is that $\Delta\bar{\nu}$ 3240 is depolarized and $\Delta\bar{\nu}$ 3418 polarized. It is necessary to reject, therefore, the hypothesis of Kastler (30) that these two bands are the *P* and *R* branches of the same oscillation. On the basis of these data, α would equal 23°. As will be seen later in a discussion of the Raman spectra of water, the specific assignment of $\Delta\bar{\nu}_1$ or $\Delta\bar{\nu}_2$ to a given Raman frequency is somewhat precarious. In applying polarization considerations to molecules of the type XY_3, where the nuclei Y may occupy the summits of an equilateral triangle, there are two possibilities, namely, the nucleus X may be on the ternary axis in the same plane as Y, or it may be outside of this plane, in which case the molecule would have a pyramid form. There are four distinct fundamental frequencies, two symmetrical and two degenerate. If the molecule is of pyramidal shape, these four frequencies are active in absorption and diffusion. If the molecule is plane, one of the symmetrical oscillations is inactive in absorption, and the other active in diffusion. The two degenerate frequencies, however, are active in absorption and inactive in diffusion. In the case of phosphorus trichloride, for example, the Raman spectrum is evidenced by four intense rays, indicating a pyramidal construction. From polarization measurements it is determined that two of these rays are polarized and two depolarized, i.e., $\rho = 6/7$ or 0.857. These are as follows:

Phosphorus trichloride

$\Delta\bar{\nu}$.	190	258	484	511
ρ..	0.90	0.29	0.86	0.14

The molecule is evidently pyramidal in construction. According to this, $\Delta\bar{\nu}$ 190 and $\Delta\bar{\nu}$ 484 are completely depolarized, corresponding to two degenerate frequencies or asymmetrical oscillations, $\Delta\bar{\nu}$ 258 and 511 corresponding to symmetrical oscillations.

TABLE 2

The degree of depolarization of some inorganic compounds

COMPOUND	ρ	$\Delta\bar{\nu}$	ρ	$\Delta\bar{\nu}$	ρ	$\Delta\bar{\nu}$	ρ	$\Delta\bar{\nu}$	ρ	$\Delta\bar{\nu}$	ρ	$\Delta\bar{\nu}$
CS_2	0 25	654	0.25	799								
SO_2	0.60	525	0.14	1145	0.80	1334						
PBr_3	0.84	116	0.18	162	0.28	380	6/7	400				
PCl_3	0.90	190	0.29	258	0.86	484	0.14	511				
$AsCl_3$	6/7	158	0 61	194	6/7	370	0 08	405				
CCl_4	0.83	218	0.79	314	0.05	458	6/7	762	6/7	790		
$SiCl_4$	6/7	151	6/7	221	0.05	425	6/7	607				
$TiCl_4$	6/7	120	6/7	144	0.05	386	6/7	497				
$SnCl_4$	6/7	105	6/7	130	0 05	368	0.63	403				
$POCl_3$	0 83	193	0.64	267	0.81	337	0.05	486	6/7	581	0.4	1290
SO_2Cl_2	0 70	214	0.93	280	6/7	365	6/7	390	0.07	408	0.06	556–563
H_2O	D	3240	P	3418								

Cabannes and Rousset (22) discuss in detail the application of depolarization measurements to the most general types of molecular configuration. The same principles apply in all cases. The measured depolarization for a number of inorganic compounds is given in table 2.

Bär (12) finds that $\Delta\bar{\nu}$ 1403 for liquid sulfur dioxide is completely unpolarized. Bhagavantam (15) determined the depolarization for carbon tetrachloride, silicon tetrachloride, titanium tetrachloride, and stannic chloride. In no case did the depolarization exceed 6/7. The same conclusion is reached by Bhagavantam and Venkateswaran (16).

Specchia (68) studied the depolarization of water. Cabannes and Rousset (21) concluded that Raman rays resulting from oscillations which do not destroy the symmetry of symmetrical models have a depolarization factor of less than 6/7. When the symmetry of the molecules is not retained during degenerate oscillations, $\rho = 6/7$, but never exceeds this value. In compounds of the type XCl_4, all Raman rays have $\rho = 6/7$, except one, whose polarization is due to the periodic contraction of the tetrahedron. Molecules of the type XCl_3 have two degenerate rays where $\rho = 6/7$ and two rays more highly polarized.

Anomalous depolarization in crystals is discussed by Cabannes (20).

The determination of the degree of depolarization of specific Raman frequencies in organic compounds is very useful in the determination of the character of the oscillation to which they owe their origin. This will be reserved, however, for discussion in a later review.

D. THE RAMAN EFFECT AND SPECIFIC HEAT CALCULATIONS

Since the Raman effect investigations have provided a mass of data regarding the fundamental oscillation frequencies of elements and compounds, it is not surprising that attempts have been made to correlate them with specific-heat data for simple substances. This has been done for both organic and inorganic compounds. The discussion contained herein will be limited to some of the inorganic aspects, and the organic aspects reserved for later publication.

Paramasivan (52) considers that the heat capacity per gram molecule for each substance is given by

$$RF_E\left(\frac{\theta}{T}\right) \tag{19}$$

where T = absolute temperature, $\theta = \frac{h}{k}\nu = 4.78 \times 10^{-11}\nu$, and F_E = the Einstein specific-heat function.

In the case of a liquid, the individual molecule possesses three degrees of freedom by virtue of its translational motion and three degrees of freedom from its rotation. Each degree of freedom has an energy given by

$$RF_D\left(\frac{\theta_m}{T}\right)$$

where F_D is the Debye specific-heat function.

The total heat capacity of a liquid may, therefore, be written in the form:

$$(C)_{\text{mole}} = 6RF_D\ (\theta_m/T) + \Sigma\ RF_E\ (\theta/T) \tag{20}$$

where the summation represents the total Einstein specific-heat functions due to all independent modes of vibration and θ_m represents the average values of $\frac{h\nu}{k}$ for the six degrees of freedom and may be evaluated by the formula of Lindemann (44).

For triatomic gases the linear model has two degrees of rotational freedom and three degrees of translational freedom. Consequently, one obtains

$$(C_{\nu_1})_{\text{mole}} = 3R + RF_E\left(\frac{\theta_1}{T}\right) + RF_E\left(\frac{\theta_2}{T}\right) + RF_E\left(\frac{\theta_3}{T}\right) \tag{21}$$

for the triangular model, and

$$(C_{\nu_2})_{\text{mole}} = \frac{5}{2}R + 2RF_E\left(\frac{\theta_1}{T}\right) + RF_E\left(\frac{\theta_2}{T}\right) + RF_E\left(\frac{\theta_3}{T}\right) \tag{22}$$

for the linear model.

Calculations for the specific heats of carbon dioxide, carbon disulfide, and sulfur dioxide, using equations 20, 21, and 22, are given in table 3.

In exceptional cases, in compiling the data used in these tables, where Raman spectra provided only some of the fundamental frequencies, recourse has been had to infra-red absorption data. In the case of multiple structure, the weighted mean is taken as the fundamental frequency, and in the case where a system is degenerate, the degeneracy has been taken into consideration.

For tetratomic molecules, the atoms are in the corners of a pyramid, and each system has six degrees of vibrational freedom.

There are four fundamental frequencies in this system, two of which are double oscillations. The heat capacity in the gaseous state may be expressed as

$$(C_v)_{\text{mole}} = 3R + RF_E\left(\frac{\theta_1}{T}\right) + RF_E\left(\frac{\theta_2}{T}\right) + 2RF_E\left(\frac{\theta_3}{T}\right) + 2RF_E\left(\frac{\theta_4}{T}\right) \quad (23)$$

TABLE 3

Specific heats of triatomic molecules

$T = 30°C.$

COMPOUND	$\Delta\bar{\nu}$			$F_E\left(\frac{\theta}{T}\right)$			$F_D\left(\frac{\theta_m}{T}\right)$	SPECIFIC HEAT	
								Calculated	Observed
CS_2 (liquid)..........	1470	200	668	0.047	0 927	0.467	0.41 or 0.99	0 218	0.237
CO_2 (gas).	2250	670	1346	0.003	0.455	0 075		0.159	0.154
SO_2 (gas)............	606	1146	1340	0.53	0.141	0.083		0.117	0 117

TABLE 4

Specific heats of tetratomic molecules

COMPOUND	$\Delta\bar{\nu}$				$F_E\left(\frac{\theta}{T}\right)$				SPECIFIC HEAT	
									Calculated	Observed
PCl_3 (117°C.).	512	260	488	190	0 753	0 926	0.774	0.956	0.118	0.119
$AsCl_3$ (217°C.).............	410	193	370	159	0.887	0 971	0.907	0 981	0.095	0 098

TABLE 5

Specific heats of pentatomic molecules

COMPOUND	$\Delta\bar{\nu}$				$F_E\left(\frac{\theta}{T}\right)$				SPECIFIC HEAT	
									Calculated	Observed
$SiCl_4$ (97°C.)	221	614	150	424	0 937	0.647	0.969	0 804	0.123	0.117
$TiCl_4$ (167°C.)....	145	494	120	382	0.981	0 810	0 985	0.880	0.108	0 125
$SnCl_4$ (157°C.)...	131	403	106	367	0.964	0.747	0 979	0.813	0.084	0.087

The calculated values for phosphorus trichloride and arsenic trichloride are given in table 4.

For pentatomic molecules the system possesses nine degrees of freedom and has four fundamental frequencies, some of which are multiple oscillations due to degeneracy. The specific heat may be calculated from

$$(C_v)_{\text{mole}} = 3R + 3RF_E\left(\frac{\theta_1}{T}\right) + 3RF_E\left(\frac{\theta_2}{T}\right) + 2RF_E\left(\frac{\theta_3}{T}\right) + RF_E\left(\frac{\theta_4}{T}\right) \quad (24)$$

In table 5 are given the values calculated for this equation.

The preceding calculations are of interest but involve a fair number of approximations, and the selection of particular fundamental frequency values has been made somewhat arbitrarily.

SUMMARY

It may be seen from the preceding discussion that Raman spectra investigations have many ramifications. They can provide information as to the possible vibrational and rotational transitions and hence information as to the molecular constitution of the more simple molecules from a purely physical point of view. On the assumption that one may apply with a certain degree of validity the equations relating atomic masses with binding force and frequency, calculations may be made as to the strength of this binding force under normal conditions from experimentally determined frequencies. The amplitude of oscillation of the atomic constituents in a given molecule can be approximated. From the magnitude of the frequency shifts, their relative intensities, their degrees of depolarization, and their number, can be estimated the molecular configuration necessary to fit these coördinates. In the case of debated structure of a given molecular species, this may provide all of the necessary information to distinguish between alternative hypotheses with a high degree of accuracy. It will be evident in the later discussion of the Raman frequency shifts for specific types of compounds how this information can be applied in the elucidation of both known and unknown molecular structures, the composition of liquid mixtures and amorphous solids, and properties of crystals and gases. In short, information valuable to the physicist, the chemist, and the crystallographer is obtainable from such investigations.

III. TECHNIQUE

Since a complete series of Raman lines appears for each exciting or incident radiation, it is highly essential that the incident light be monochromatic. The modified lines or Raman lines are each individually extremely weak as compared to the original source of excitation, so that it is also essential to have great intensities of exciting light and efficient optical systems. It is in this direction—namely, toward monochromatism and adequate intensities—that the major developments in technique have taken place. The most common source of light is the mercury arc; the helium lamps suggested by Wood (103, 104, 105) are more or less impracticable except in special instances. The mercury arc provides three lines of importance, the 4358, 4047, and the 2536 A.U. lines. The use of the 4358 A.U. is quite general, but its utility depends on the elimination of the 4047 A.U. as a simultaneous source of energy.

The failure so to eliminate the 4047 A.U. leads to discordant results which will be discussed later. In addition to these difficulties there is a continuous spectrum from the mercury arc which must be likewise diminished. The standard filter for the removal of the 4047 A.U. line has been an acid solution of quinine sulfate, which, however, has the disadvantage of decomposing on prolonged exposures. Pfund (100) found that a 12-mm. layer of a saturated solution of sodium nitrite shows a 65 per cent transmission of the 4358 A.U. and 1 per cent of the 4047 A.U. lines. Likewise, *m*-dinitrobenzene (81, 90) transmits the greater portion of the 4358 A.U. and little of the 4047 A.U. line. It must be frankly admitted that there is no perfect system and any monochromatic gains are at the sacrifice of some intensity. Krishnamurti (96) has suggested sodium salts of *o*-cresolphthalein for the isolation of the 4047 A.U. mercury line. Corning Red Purple Ultra glass is about as efficacious for this purpose as any filter. For the isolation of the 2536 A.U. mercury line, Bolla (84) used a mercury vapor filter to prevent halation, and Hulubei (92) used chlorine under pressure.

The use of Corning glass Noviol O to eliminate the 3650 A.U. mercury lines, concentrated praseodymium solutions to eliminate some of the halation from the 4358 A.U. mercury line, and a solution of iodine and carbon tetrachloride as a filter to reduce the 4358 A.U. mercury line in favor of the 4047 A.U. mercury line, as well as improved optical arrangements, have been suggested by Wood (106, 107, 108). To increase the intensity of light used for special excitation purposes, lamps other than mercury arcs and especially designed mercury lamps have been employed. Krishnamurti (95) used a cadmium arc (82) containing 50 per cent tin. This gave as exciting lines 4800 A.U., 5086 A.U., and 6438 A.U. A simple capillary fused silica mercury lamp has been described by Daniels and Heidt (87). Lamps similarly constructed but developed to use metals other than mercury, such as bismuth, cadmium, lead, thallium, and zinc, have been constructed by Hoffman and Daniels (91). A special mercury lamp designed with a discharge surrounding the material to be investigated is described by Venkatesachar and Sibaiya (71). This is similar to the lamp previously developed by Bates (102) for photochemical studies. A spiral mercury lamp for the study of crystals has been developed by Hibben (89). A hot cathode helium lamp in a reflecting apparatus so arranged that the Raman tube is at one of the foci of the ellipse, the helium lamp at the other, has been described by Buttolph (86).

To accomplish much greater increases in effective intensity, more efficient optical systems are necessary. They have been discussed by Anand (79, 80), Almasy (78), Grassmann (88), and Mesnage (98). The filling up of the spectrogram with light has been considered as a geometrical problem by Nielsen (99). Other improvements have been suggested by Hulubei and Cauchois (93, 94) and by Ziemecki (109).

A rapid spectrograph of high dispersion for Raman effect studies in the visible region of the spectrum has been designed by Bourguel (85).

A special apparatus for studying the Raman effect in liquids at liquid air temperatures has been described by McLennan, Smith and Wilhelm (97).

Typical apparatus used for the investigation of the Raman effect of gases under pressure has been designed by Bhagavantam (83) and Rasetti (101).

Development in technique of Raman effect applications has been relatively slow. This is partially because some results are obtainable under almost any circumstances. The importance of further necessary improvements cannot be overestimated. The scope and the accuracy of future observations are in a large measure dependent on the refinements in procedure already developed and in the continued improvement of the experimental method.

IV. Raman Spectra of Inorganic Crystals

The Raman effect in inorganic crystals serves the purpose of determining the Raman shifts for compounds whose structures and compositions are sometimes known since there are three other independent sources of information concerning them, namely, analytical, crystallographic, and x-ray. With a partially identified constitution, therefore, the Raman lines obtained from such investigations can be attributed with some degree of certainty to definite interatomic oscillations and configurations. This is a mandatory preliminary for the study of the Raman effect in solutions. If the Raman lines given by a group are determined in the crystalline form and the same lines persist when the crystal is dissolved, then it is not unreasonable to suppose that the same group or groups persist in solution. For example, if the Raman lines of a series of nitrites are determined in crystalline form and the same lines persist in the aqueous solution of these substances, this is *a priori* evidence that the nitrite exists *as such* in solution. Conversely, variations from these determinations are *a priori* evidence that modification of the solute in solution exists. This application will be discussed further in the consideration of the Raman effect of acids, alkali solutions, and intermediate compounds. The interpretation of the Raman effect in amorphous solids is likewise predicated upon a similar phenomenon.

Large numbers of crystals were examined prior to 1931. It would serve no useful purpose to repeat many of these. There are some, however, somewhat out of the ordinary, which might be advantageously mentioned.

Chlorates, bromates, iodates, tungstates, molybdates, perchlorates, and periodates

Krishnamurti (134) found for $NaClO_3$, $KClO_3$, $Ba(ClO_3)_2 \cdot H_2O$, $NaBrO_3$, $KBrO_3$, KIO_3, HIO_3, $NaClO_4 \cdot H_2O$, NH_4ClO_4, KIO_4, $(NH_4)_6Mo_7O_{24} \cdot 4H_2O$, $PbMoO_4$, $CaWO_4$, and $Na_2WO_4 \cdot 2H_2O$ the principal Raman shift $\Delta\bar{\nu}$ 930 of the chlorates to be represented by two shifts 770 and 842 in the bromates and by four, 733, 751, 784, and 801 in the iodates. The perchlorates give Raman lines at 462, 633, and 933. The molybdates give shifts of 932 and 880; the tungstate 928.

For crystalline sodium bromate Schaefer, Matossi, and Aderhold (156) observed $\Delta\bar{\nu}$ 357, 370, 799, and 836, $\Delta\bar{\nu}$ 799 being very strong, and for cadmium bromate $\Delta\bar{\nu}$ 787.

Sulfates

The frequency shifts for fifteen crystalline inorganic sulfates were determined by Krishnamurti (133). These comprised iron, nickel, ammonium, zinc, copper, potassium, magnesium, mercury, barium, manganese, sodium, strontium, cadmium, calcium sulfates, and potassium alum. The magnitude of the shifts depends somewhat on the cation. On the average they correspond to $\Delta\bar{\nu}$ 454, 625, 990, and 1120. Not all of these frequencies were found, however, for each element examined.

More recently, Nisi (146) determined the Raman spectra of the sulfate crystals of lithium, sodium, potassium, rubidium, ammonium, beryllium, magnesium, zinc, cadmium, calcium, barium, strontium, copper, nickel, iron, manganese, potassium alum, ammonium iron sulfate, and sodium thiosulfate. On the average the $\Delta\bar{\nu}$ obtained from these crystals were 415, 462, 619, 986, 1006, 1076, and 1125. Of these shifts those near $\Delta\bar{\nu}$ 1000 were strong, and $\Delta\bar{\nu}$ 462 and 671 diffuse and of medium or less intensity. Copper sulfate showed a number of lines between $\Delta\bar{\nu}$ 84 and $\Delta\bar{\nu}$ 280.

Sodium thiosulfate pentahydrate gave $\Delta\bar{\nu}$ 324, 434, 546, 612, 674, 1018, 1116, 1163. Of these $\Delta\bar{\nu}$ 434 was classed as very strong and $\Delta\bar{\nu}$ 1018 medium.

The spectrum of the deformed sulfate ion is compared with that of a regular tetrahedron by Cabannes (113), who obtained for calcium sulfate dihydrate (gypsum) $\Delta\bar{\nu}$ 414, 495, 620, 671, 1109, and 1133. The shift $\Delta\bar{\nu}$ 671 is anti-symmetrical to the binary axis *L*. Gypsum and barite ($BaSO_4$) were also investigated by Rasetti (153). Hollaender and Williams (127) obtained $\Delta\bar{\nu}$ 696, 980, and 1128 from gypsum and $\Delta\bar{\nu}$ 461, 702, and 980 from barite.

Nitrates

The nitrates have been studied extensively. Menzies (142) obtained $\Delta\bar{\nu}$ 1052 for potassium nitrate, using coarse crystals. Bär (110) obtained the Raman spectra of sodium, ammonium, and calcium nitrates. Ammonium nitrate gave $\Delta\bar{\nu}$ of 706 and 1056; calcium nitrate, 1054; and sodium nitrate, 1074.

Krishnamurti (135, 130, 137) investigated some eighteen nitrates. The strongest line identified as the inactive frequency of the nitrate ion (116) varies from 1030 to 1066, depending upon the cation. Other lines were present for the nitrates of the alkalies and some of the alkaline earths. On an average, these were $\Delta\bar{\nu}$ 185, 725, 1380.

Nisi (148) examined single crystals of sodium nitrate and obtained $\Delta\bar{\nu}$ 101, 189, 723, 1067, 1385, and 1666. Under like conditions he obtained the following results: For potassium nitrate, $\Delta\bar{\nu}$ 31, 51, 84, 711, 1048, and 1344; for rubidium nitrate, $\Delta\bar{\nu}$ 109, 147, 705, 1056, and 1364; for cesium nitrate, $\Delta\bar{\nu}$ 116, 149 (?), 715, 1050, and 1346; and for ammonium nitrate $\Delta\bar{\nu}$ 59, 86, 142, 170, 714, 1041, 1869.

Single crystals of sodium nitrate, crystallized from the molten solution, give $\Delta\bar{\nu}$ 103, 190, 730, 1074, 1391, and 1678. The first two of these were considered by Cabannes and Canals (114) as external frequencies, the succeeding three as fundamental frequencies, and $\Delta\bar{\nu}$ 1678 as a combination frequency. Of these fundamentals, $\Delta\bar{\nu}$ 730 and 1391 are active and $\Delta\bar{\nu}$ 1074 inactive.

Nitrites

For sodium nitrite, Carrelli, Pringsheim and Rosen (116) obtained $\Delta\bar{\nu}$ 696, 785, 1303. Bär (110) obtained $\Delta\bar{\nu}$ 1333.

Halogen compounds

Crystalline inorganic chlorides containing more than one atom in the anion have been investigated by Krishnamurti (131) and the following $\Delta\bar{\nu}$ were obtained: $HgCl_2$, 313, 381; Hg_2Cl_2, 165, 273, 295, 320; $ZnCl_2$, 234; CdI_2, 105, 345, 395; $SbCl_3$, 145, 166, 312, 337; $BiCl_3$, 153, 169, 242, 288; PCl_5, 248, 356, 405, 450.

Krishnamurti (136) found that the Raman spectrum of mercuric chloride gives a strong line at $\Delta\bar{\nu}$ 313 and a fainter at 381, whereas mercuric bromide gives only one at $\Delta\bar{\nu}$ 187.

The Raman spectrum of sodium chloride has been sought by Fermi (118) and by Fermi and Rasetti (119). The effect in this case is extremely weak and is considered a Raman effect of the second order.

Haun and Harkins (123) found germanium tetrachloride to yield Raman lines at $\Delta\bar{\nu}$ 132, 171, 397, and 451. The first two are optically active and the other two inactive.

The Raman spectra of aluminum chloride $\Delta\bar{\nu}$ 541 and 806 (125), sodium silicate, orthophosphoric acid, and potassium hydrogen phosphite were determined by Hibben (124).

The Raman spectra of fluorite, anhydrite, rock salt, and ice have been investigated by Rasetti (152, 153), using the 2536 A.U. line of mercury as the primary radiation. New bands were observed. The Raman effects of molecules of XY_6 and XY_5, such as $HSbCl_6$ and H_2SnCl_6 and $SbCl_5$ were investigated by Redlich (154).

The large frequency shifts of $\Delta\bar{\nu}$ 7256 and 7270, respectively, found by Rasetti (151) in fluorite and calcite have been attributed by Tomaschek (157) to the phosphorescent lines of gadolinium, known to be present in natural fluorite.

Silicates and phosphates

The fundamental frequencies of the SiO_4 group in quartz crystals have been determined by Weiler (158). These are $\Delta\bar{\nu}$ 502, 800, 1062–1086, 1170–1208. With the aid of these, the entire infra-red spectrum below 10μ can be interpreted as a system of combination bands of the second to the fourth order. A study was also made of polymeric homologous series of silica esters (159, 160). In these compounds four characteristic scattered frequencies must be attributed to SiO_4.

The average shifts obtained from quartz, SiO_2, were $\Delta\bar{\nu}$ (85),[1] (106), 127, 207, 267, (321), 355, 404, 465, 702, (740), 802, 1070, (1111), 1164, 1227. The investigation of quartz has been conducted by Landsberg and Mandelstam (37, 140, 141), Hollaender and Williams (126, 127), Gross and Romanova (122), Pringsheim and Rosen (149), Wood (161), Menzies (143), Daure (24), Ney (47), Krishnan (138, 139), Nisi (144, 145), Rao (150), Brickwedde and Peters (18), and Rasetti (153). Of the shifts given $\Delta\bar{\nu}$ 127 and $\Delta\bar{\nu}$ 465 are strong.

The Raman effect in phosphates and silicates was investigated by Nisi (147). The Raman spectra of apatite, beryllonite, phenacite, topaz, beryl, danburite, zircon, and tourmaline were examined in detail. The following $\Delta\bar{\nu}$ were observed: For apatite, $Ca_5(F, Cl)(PO_4)_3$, $\Delta\bar{\nu}$ 442, 592, 966, and 1044 ($\Delta\bar{\nu}$ 966 strong); for beryllonite, $BeNaPO_4$, $\Delta\bar{\nu}$ 232, 354, 416, 463, 572, 612, 1010, 1045, and 1070 ($\Delta\bar{\nu}$ 1010 strong); for phenacite, Be_2SiO_4, $\Delta\bar{\nu}$ 219, 378, 444, 523, 876, 915, 947, 1014 ($\Delta\bar{\nu}$ 876 strong); for topaz, $Al(F, OH)_2SiO_4$, illuminated parallel to the $z(y)$ axis, $\Delta\bar{\nu}$ 243, 270, 288, 336, 393, 520, 560, 857, 925, 983, 1007, 1165, (3649) ($\Delta\bar{\nu}$ 925, 270 strong); for beryl, $Be_3Al_2Si_6O_{18}$, $\Delta\bar{\nu}$ 318, 393, 424, 450, 528, 624, 684, 1012, 1074, 1243, 1390, 1519, (3607) ($\Delta\bar{\nu}$ 684 strong); for danburite, $CaB_2Si_2O_8$, $\Delta\bar{\nu}$ 92, 124, 186, 207, 242, 269, 289, 342, 371, 422, 608, 884, 970, 1110, 1158, 1205 ($\Delta\bar{\nu}$ 608 strong); for zircon, $ZrSiO_4$, $\Delta\bar{\nu}$ 355, 438, 1006 ($\Delta\bar{\nu}$ 1006 strong); for olivine, Mg_2SiO_4, $\Delta\bar{\nu}$ 146, 827, 856 (all doubtful). For topaz the intensity of the Raman lines is a function of the direction of observation and illumination.

Krishnan (139) observed $\Delta\bar{\nu}$ 1053 for topaz.

Carbonates

Magnesite ($MgCO_3$) gives $\Delta\bar{\nu}$ 1098, and cerussite ($PbCO_3$) $\Delta\bar{\nu}$ 59, 74, 102, 118, 146, 177, 1052, 1363, and 1476 as observed by

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[1] A wave number shift in parentheses indicates some doubt as to its numerical value or as to its existence.

Schaefer, Matossi, and Aderhold (156). In the latter compound the two lowest frequencies, as well as $\Delta\bar{\nu}$ 1052, are strong.

Aragonite ($CaCO_3$) has been investigated by Kimura and Uchida (128, 129), Schaefer, Matossi, and Aderhold (156), Bhagavantam (112), Nisi (148), and Rasetti (153), who obtained $\Delta\bar{\nu}$ 94, 156, 209, 271, 708, and 1087 for average values.

Calcite ($CaCO_3$) has been extensively investigated by Landsberg and Mandelstam (37, 140, 141), Wood (161), Kimura and Uchida (129), Krishnan (139), Nisi (144), Schaefer, Matossi, and Aderhold (155, 156), Daure (24), Embirikos (117), Venkatesachar and Sibaiya (71), Bhagavantam (112), Rasetti (151), Cabannes and Canals (114), Cabannes and Osborne (115), and Rasetti (153). On the average the following $\Delta\bar{\nu}$ were obtained: 132, (147), 155, (161, 221), 282, 714, (771, 877), 1088, (1438), (1747), (7270, 7345, 7395, 7456). The frequency shifts indicated in parentheses are doubtful, particularly the four large frequency shifts.

Hydroxides

Krishnamurti (96) found that crystalline sodium hydroxide gives a strong sharp line at $\Delta\bar{\nu}$ 3630, which is attributed to the OH ion.

Sulfur and phosphorus

Irradiating sulfur crystals at liquid air temperatures, Krishnamurti (136) has obtained four Raman lines corresponding to $\Delta\bar{\nu}$ 151, 218, 447, 475, all of which are strong except $\Delta\bar{\nu}$ 447.

Three Raman shifts are obtained from yellow phosphorus, $\Delta\bar{\nu}$ 374, 468, and 607 (111).

The Raman effect of crystals of PH_4I has been studied by Gopal Pai (121), with a view to correlating it with the crystal structure of the compound. The $\Delta\bar{\nu}$ found are 930, 1040, 1130, 1259, 1416, 2304, 2370. All these frequencies were attributed to the ionic group PH_4.

SUMMARY

Some of the material in the foregoing has been included not only because of its intrinsic interest but also as a matter of reference standard for the discussion on solutions.

No attempt has been made to indicate, except in a general manner, the relative intensities, regardless of the fact that intensity is one of the factors necessary to the full description of a Raman shift. This is for two reasons: in practically no case has the intensity been measured by microphotometric means; and the halation due to general scattering makes visual estimates only very roughly approximate. Very marked differences in intensity are, however, easily discernible.

The crystalline compounds examined comprise most of the more common types of inorganic salts. In a given type group, there are some regular differences which are reasonably noticeable. It should be borne in mind, however, that generally a difference of a few wave numbers may be well within the experimental error in measuring the magnitude of the displacement. Measurements by different observers will often produce a difference in estimating the maximum of a few wave numbers.

As pointed out by Krishnamurti, the displacement of the strongest line characteristic of the SO_4 group near $\Delta\bar{\nu}$ 1000 is a function of the cation, decreasing with increasing volume of the cation, e.g., $\Delta\bar{\nu}$ for sodium 995, potassium 981, ammonium 974. This depends, however, upon the particular group of the periodic system in which a given series lies. For calcium the shift is $\Delta\bar{\nu}$ 1008, strontium 999, and barium 988.

In the tetrahedron model suggested for the SO_4 group, the $\Delta\bar{\nu}$ 1120 and 625 are taken as active frequencies and $\Delta\bar{\nu}$ 990 and 454 are inactive ones. The SO_4 group may be easily deformable, as is evidenced by the variable nature of the positions and intensities of the lines (133), and it may therefore depart, to a considerable extent, from a tetrahedral symmetry.

Another striking fact which emerges from this investigation is that this shift ($\Delta\nu$ 990) is very much weakened in substances which have a large paramagnetic susceptibility, in this case iron, nickel, copper, and manganese. All diamagnetic sulfates show this line prominently.

Nisi (146) takes exception, however, to this observation regarding paramagnetic crystals. He obtained for $FeSO_4 \cdot 7H_2O$ a line of medium intensity at $\Delta\bar{\nu}$ 984 and a faint one at 1096. For

$MnSO_4 \cdot 7H_2O$ two lines were observed, $\Delta\bar{\nu}$ 994 and 1087, and for $NiSO_4 \cdot 7H_2O$, one line at 985. In addition to this he observed that the more complicated sulfates, such as $CuSO_4 \cdot 5H_2O$, tend to have more complicated Raman spectra, the lines corresponding to active vibrations splitting into doublets or triplets, the higher frequency shift component being the more intense. In the series lithium, sodium, potassium, rubidium and ammonium sulfates the frequency shift of the inactive line near $\Delta\bar{\nu}$ 1000 decreased as the cation volume increased. The spectrum obtained from gypsum ($CaSO_4 \cdot 2H_2O$) showed considerable variation in the intensity of this line ($\Delta\bar{\nu}$ 1000) depending upon the direction of illumination and observation. Roughly speaking, in the cases of illuminations from the direction parallel to the $b(y)$ axis and observed from various directions, the intensity of one component of the doublet $\Delta\bar{\nu}$ 415 and 493 reaches a maximum and that of the other a minimum, and *vice versa*, when these two directions are nearly perpendicular to each other.

The strongest line for the nitrates, as previously mentioned, is that which corresponds to the inactive frequency of the nitrate ion. According to Krishnamurti (130), the latter corresponds to a symmetrical vibration of the three oxygen atoms toward and away from the central atom, producing no change in electrical moment. The oxygen atoms occupy the corners of a plane equilateral triangle with the nitrogen atom at the center. The vibration corresponding to $\Delta\bar{\nu}$ 725 is due to the movement of any one oxygen atom along the median followed by a small alternate elongation and diminution of the opposite side of the group (this may also be considered a drum-head vibration of the ion, the nitrogen atom vibrating perpendicularly to the plane), while the shift at $\Delta\bar{\nu}$ 1380 is due to the oscillation of the nitrogen atom along or perpendicular to any median. As in the case of the sulfates, there is a slowing down of the oscillation frequency with the increase in atomic weight of the metal ion (120). It was observed that lithium, sodium, and magnesium nitrates showed a fairly large frequency shift (maximum value $\Delta\bar{\nu}$ 1069), while calcium, barium, lead, potassium, aluminum, cadmium, and silver showed intermediate values, the smaller shifts (minimum value $\Delta\bar{\nu}$ 1037) being exhibited by lead, mercury, and bismuth. The view was put forth that, in the fully ionized crystals, the influence of the cation on the vibration of the anion is proportional to the volume occupied by the cation in the crystal lattice, although in this case this is disputed by Nisi (148). The smaller the volume, the greater the characteristic oscillation frequencies associated with the nitrate group.

Only two out of the three active frequencies of the nitrates recorded by infra-red measurements appear as Raman lines. One of these is, on the average, $\Delta\bar{\nu}$ 725. For the alkali metals this shift also decreases with increased volume of the cation. But with barium and lead nitrates a too large frequency shift was observed. It was concluded that the frequency observed with the alkali nitrates is different in origin from those observed with strontium, barium, and lead nitrates. With the former compounds, it was postulated that the vibrations are in the plane of the NO_3 group, while with the latter the $\Delta\bar{\nu}$ probably represent vibrations of the nitrogen atom at right angles to the plane. This explanation is a matter of opinion.

The second active frequency, $\Delta\bar{\nu}$ 1380, is more a broad band with the higher nitrates than with lithium and sodium, for example. The actual maximum changes little. The lowest frequency shift, $\Delta\bar{\nu}$ 185 (on the average), varies considerably from compound to compound. Krishnamurti attributes this to a lattice vibration probably involving mutual swings between the nitrate ion and the cation. Its frequency is greater for a smaller cation. This vibration disappears in solution.

The halides may be classified, according to Krishnamurti (132), into three groups: (a) those that show strong Raman lines, for example, the chlorides of Hg, P, As, Sb, C, Si, Ti, Sn, and H; (b) those that show faint Raman lines, $BiCl_3$, $ZnCl_2$, CdI_2, $AuCl_3$; (c) and those that show no Raman lines at all, chlorides of Na, K, NH_4, Ba, Ag, Cu, Cd, Mg, Sn (ous), Th, and Cd, Br_2, PbI_2, KI, LiF, NaF, CaF_2. It is postulated that these distinctions are dependent upon the type of binding, that is, either ionic or covalent. Those halides that are good conductors show no Raman spectra, while those that are nonconductors or feeble conductors show Raman lines more or less strongly. Mercuric chloride, for example, is very little ionized in solution, and the conductivity of the molten substance is very low. This compound has one strong line, $\Delta\bar{\nu}$ 312, and a faint companion line at $\Delta\bar{\nu}$ 381. It is assumed that the strong line represents a symmetrical vibration of the chlorine atoms towards and away from the central atom in a linear model for the mercury molecule. This bears some similarity to the vibrations of carbon dioxide and carbon disulfide. The weak line is attributed to the oscillations of the chlorine atom against the remainder of the molecule.

The Raman spectrum of mercurous chloride cannot be explained on the basis of a simple HgCl molecule. The stronger line for this substance, $\Delta\bar{\nu}$ 275, is attributed to the symmetrical movement of the chlorine atoms towards and away from the central Hg–Hg group in a linear model

The broad division between ionic and molecular lattices finds a counterpart in the Raman spectra in typical ionic crystals, such as sodium chloride, which shows no vibrational Raman spectrum, while typical molecular substances show prominent lines. Compounds of the type of cadmium iodide probably belong to the transition stage.

While the most abundant naturally occurring crystals are silicates, their very complexity has been something of a deterrent from the point of view of Raman spectra investigations. It has already been pointed out that this method of approach is somewhat empirical in nature, particularly in the case of complicated compounds. It has been necessary, therefore, to lay a substantial foundation before approaching complex silicates.

Nisi (147) points out that according to x-ray analysis in the orthosilicates the SiO_4 group is independent, each oxygen atom combining with one silica atom, as well as being linked to other metal ions, by which the groups are bound together. In other silicates one or more of the four oxygen atoms are shared by two silicon atoms and form silicon–oxygen complexes.

The strongest frequency obtained on examination of the compounds previously mentioned is attributed to the inactive vibration of the SiO_4 group and increases with the valency of the metal ion as observed in the cases of the sulfates and nitrates. A large frequency shift was noted at about $\Delta\bar{\nu}$ 3650, the origin of which is as yet unknown. A large number of Raman shifts were obtained from most specimens, but the experimental data are too scattered as yet to find any definite relations between crystal structures and the frequency shifts of the Raman lines.

Those minerals containing a PO_4 group have a strong Raman line corresponding to an inactive frequency shift near $\Delta\bar{\nu}$ 1000. The shift is somewhat smaller in the case of the sulfate, notwithstanding the fact that the phosphorus atom is lighter than the sulfur atom. As is to be expected, the PO_4 group shows other similarities with the SO_4 group.

On the whole there is essentially little difference between the Raman spectra from aragonite and from calcite. There may be some differences in intensities. Apparently $\Delta\bar{\nu}$ 188 in calcite is stronger than the equivalent shift in the aragonite. The ratios of intensities of the lines corresponding approximately to $\Delta\bar{\nu}$ 278 and $\Delta\bar{\nu}$ 156 are in a reverse order in the two crystal planes (148). Most of the apparent differences, if any, owe their origins to faint lines which by different observers may be evaluated differently.

As will be seen later, the spectrum of the crystalline hydroxides is consistent with the view that $\Delta\bar{\nu}$ 3630 arises from the oscillation of the hydrogen atom against the oxygen atom. In the solid this vibration is appreciably sharper than in the liquid or in solution. Unfortunately, other than sodium hydroxide, most of the hydroxides investigated have been in the form of the crystal hydrates. This has resulted in a confusion between the $O \leftrightarrow H$ vibration of the true hydroxide and that arising from the water of crystallization.

The Raman spectra of inorganic crystals provide, as may be seen, some information concerning the type of interatomic binding, the crystal structure that may be expected, and reference points from which the Raman spectra of solutions and complexes may be more advantageously studied.

V. RAMAN SPECTRA OF WATER

Perhaps the most consistently divergent results with any compound have been obtained in the Raman spectra studies of water. This is attributable to two factors: first, the bands are broad and diffuse and it is difficult to estimate the various maxima; second, the actual magnitudes of the frequency shifts apparently depend on the previous history of the water. This is not unreasonable from a physico-chemical point of view, as water has long been thought to consist of more than one elementary form, usually termed the mono-, di- and tri-hydrol forms, depending on whether the water is polymerized into one, two, or three molecular units. The maximum polymerization has been supposed to occur at the lower temperatures. Regardless of the disagreement among the various observers as to the magnitude of the frequency shifts observed with water, there is a fairly uniform consensus of opinion that the intensity of the maxima is a function of temperature. Furthermore, there is an additional change in aqueous solutions, depending on the solute.

Rao (150) obtained average maxima for water at $\Delta\bar{\nu}$ 3345 and for ice $\Delta\bar{\nu}$ 3223. Later he recorded for water (181) three bands: $\Delta\bar{\nu}$ 3205, 3410, 3582. The first of these decreases in intensity with increasing temperature and the last increases, the middle band remaining constant. The addition of electrolytes causes similar behavior. Ice shows the opposite intensity relations; the $\Delta\bar{\nu}$ 3205 in ice has greater intensity than in water, and the 3582 weaker than in water.

Gerlach (167) and Pringsheim and Schlivitch (178) made similar observations.

Meyer (175) accounted fairly plausibly for the increased broadening and dissymmetry of the water band with increasing temperature on the assumption that water is a mixture of di- and tri-hydrols at lower temperatures, the tri-hydrol being more abundant.

Ganesan and Venkateswaran (166) obtained for water $\Delta\bar{\nu}$ 2355, 3199, 3453, 3609, and 5502, the 2355 band being doubtful. At 80°C. the 3199 band practically disappears, while the 3453 and 3609 bands diminish only slightly in intensity. The decrease in the 3199 band was attributed to depolymerization. For ice these authors found $\Delta\bar{\nu}$ 3193, 3391, 3549, 5393, each band being more narrow than in the case of water. In the case of ice the 3193 and 3391 bands are of approximately the same intensity. With water the 3453 band is more intense than the former. The 5393 band is much brighter in ice than it is in water.

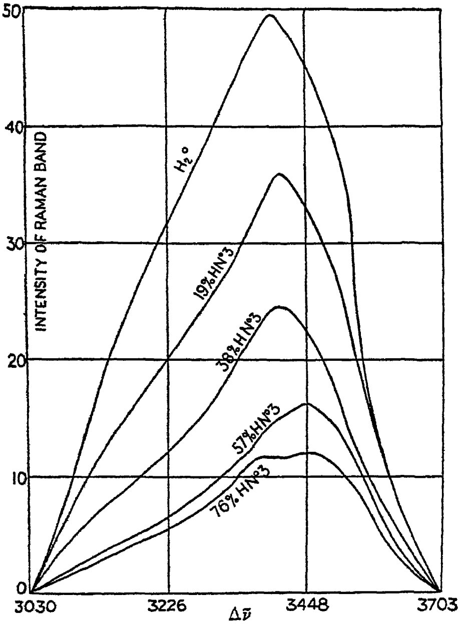


FIG. 8. THE EFFECT ON THE WATER BANDS OF DIFFERENT CONCENTRATIONS OF NITRIC ACID

A splitting of the water band near $\Delta\bar{\nu}$ 3448 into at least two maxima is shown (after Rao).

Rao (182) studied the Raman spectrum of water as a function of temperature, and water solutions of nitric acid as a function of concentration. For pure water he obtained maximum values at $\Delta\bar{\nu}$ 3085, 3420, and 3635. The distribution of intensity in the water bands at 14°C. and 75°C. was determined. With increased temperature there is a diminution of intensity in the 3085 band and an increase in intensity in the 3635 band. This change was again attributed to a change in the relative proportions of water polymers. According to Rao, a change in the maximum of the 3420 band toward a higher frequency would also indicate a decrease in the number of double molecules.

The changes in intensity distribution with the addition of an electrolyte may also be due to the diminution of the proportion of the triple molecules and to the increase of the single molecules. With high concentrations of nitric acid (76 per cent), however, a second maximum begins to develop which does not appear in the temperature phenomenon (figure 8). This was ascribed to the formation of hydrates; the water molecules, instead of combining among themselves, begin to associate with the molecules of the electrolyte. The heaviness of the ions or molecules with which the water molecule combines results in only a small shift of the water band; hence a second maximum in nitric acid at about 3400 was observed.

Brunetti and Ollano (164) and Ollano (177) stated that the water bands are composed of three elements corresponding to $\Delta\bar{\nu}$ 3225, 3469, 3589, the 3469 being the most intense. These authors stated that the triangular water molecule should have three fundamental frequencies, the absorption spectra indicating two fundamentals, one at $\Delta\bar{\nu}$ 1640 and another at $\Delta\bar{\nu}$ 3360, the third being inactive. If this is true, the inactive frequency should appear in the Raman effect the same as the inactive frequencies of carbonate and nitrate ions. No Raman line at $\Delta\bar{\nu}$ 1640 was observed. The $\Delta\bar{\nu}$ 3225 was attributed to the most polymerized state of water and the $\Delta\bar{\nu}$ 3589 to the least or to water itself. Solutions containing hydrochloric acid or cesium chloride cause a decreased intensity of the 3225 and 3589 bands, while the 3469 band is intensified. This behavior is accounted for on the basis of chloride ions causing a depolymerization of the higher polymers and an increased polymerization of the lighter polymers. In nitrate solutions the 3589 band increases so much in intensity that the middle line $\Delta\bar{\nu}$ 3469 loses its identity. $\Delta\bar{\nu}$ 3225 weakens slowly under these conditions and is absent only in solutions of high concentration. It is concluded that in the presence of the nitrate ion the aqueous solvent depolymerizes but does not become homogeneous.

Segré (183), by excitation with the 2536 A.U. mercury line, which is reabsorbed by mercury vapor, observed a new water band with a maximum displacement of Δν̄ 140, both as Stokes and anti-Stokes lines. Since this can not be attributed to rotational or vibrational spectra of hydrogen, it was ascribed to the oscillations of the water polymers. On increasing the temperature from 20°C. to 90°C. there is a decrease in intensity of this band (figure 9). Another weak and diffuse band, also sensitive

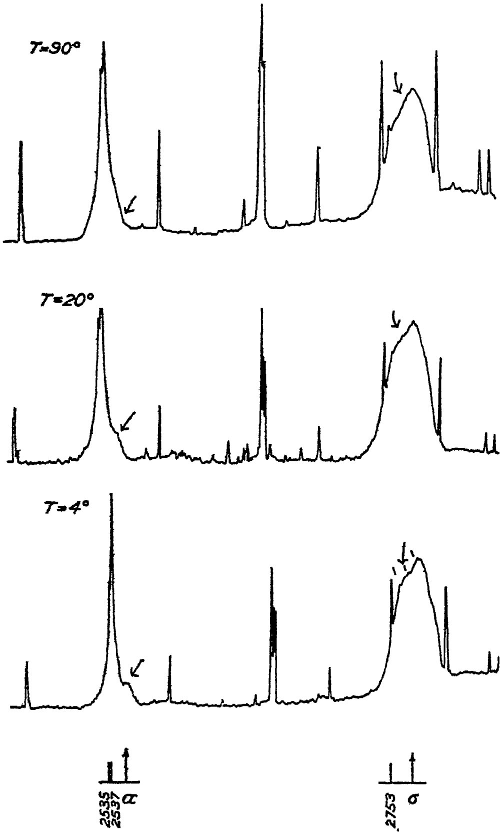


FIG. 9. THE MODIFICATION OF THE WATER BANDS WITH CHANGING TEMPERATURE

Showing a diminution with increased temperature in the intensity of Δν̄ 140, and the three bands near Δν̄ 3220, 3445, and 3630 (after Segré).

to temperature at about Δν̄ 600, was observed. The 140 shift is not present in ice. Since the latter is also presumed to be polymerized, this seems somewhat inconsistent.

This low frequency oscillation has also been observed by Bolla (84). The frequency shift has been given, however, as Δν̄ 172 instead of 140. In addition two new lines at Δν̄ ±60 were observed with the same technique as used by Segré (figure 10). Both Stokes and anti-Stokes lines were observed in all cases. The larger frequency shifts obtained were Δν̄ 3220, 3445, and 3630. These are shown in figure 11.

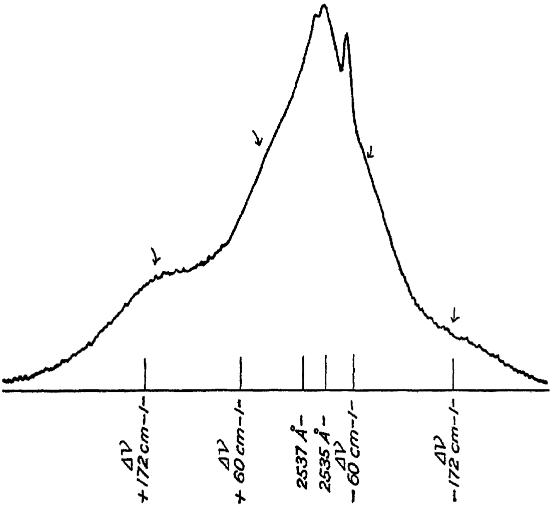


Fig. 10. Low-Frequency Oscillations in Water Attributed to the Polymers of Water
(After Segré)

In addition to these bands Bolla (163) more recently has observed in water at 17°C. Δν̄ 510, 780, 1645, 2150, and 3999, all being very weak, but of this group of lines Δν̄ 1645 is the strongest. Magat (170) reports Δν̄ 190 and 600 as present in water and states that if the three fundamental frequencies of water are Δν̄ 600, 1595, and 3500 it is possible to interpret the absorption spectrum as a combination of fundamental frequencies and their harmonics.

On the basis of quantum mechanics supplemented by spectroscopic data, Van Vleck and Cross (187), Mecke (171) and Mecke, Baumann, and Freudenberg (172, 173, 174) have calculated two of the fundamental frequencies of the water to be near Δ$\bar{\nu}$ 3600 and 3750, the diffuseness of the bands being attributed to a superposition of the vibrations. The third calculated fundamental lies near Δ$\bar{\nu}$ 1660. Johnston and Walker (169) measured the Raman spectra of water vapor at 275°C. and observed Raman shifts at Δ$\bar{\nu}$ 3654, 1648, and 984, the last fundamental being inconsistent with the calculations just mentioned. It is to be remembered that these latter involve considerable approximations and are for isolated molecules. The shift at Δ$\bar{\nu}$ 1654 has been observed by Silveira (184) in the Raman spectrum of salt solutions and was tentatively attributed by him to the water molecule. It is, however, exceedingly weak, and its reality not conclusively established.

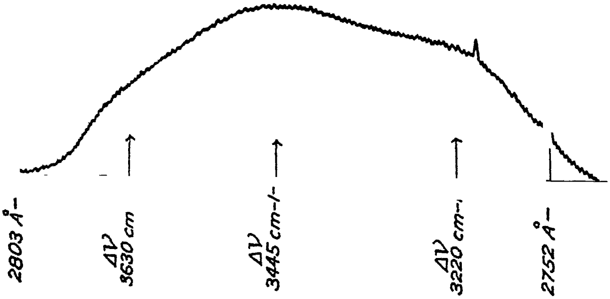


Fig. 11. High-Frequency Oscillations in Water
(After Segré)

Rank (180) observed Δ$\bar{\nu}$ 3650 in water vapor but could not find Δ$\bar{\nu}$ 984 and Δ$\bar{\nu}$ 1648. The shift Δ$\bar{\nu}$ 984 observed by Johnston and Walker was attributed to a shift of Δ$\bar{\nu}$ 3650 excited by the 3906 A.U. mercury line. The frequency shift Δ$\bar{\nu}$ 3654 has also been observed by Daure and Kastler (165) in water vapor.

The largest number of Raman lines for water have been observed by Hulubei (92). He obtained two frequency shifts, Δ$\bar{\nu}$

3233 weak and 3443 strong. No third component was observed. He attributed a third band found by others to imperfect monochromatism in the exciting sources. In addition to these bands a number of other Raman lines were observed which are represented to be combinations of the fundamental frequencies obtained in infra-red absorption corresponding to 6.26 μ and 2.66 μ (ν_1 and ν_2). These are as follows:

$\Delta\bar{\nu}$......	6747	7246	7757	8200	8660	9175	9569	10039	10635	10944
μ........	1.48	1 38	1.29	1.21	1.154	1.09	1.05	0.99	0.94	0 91
	$2\nu_1 + \nu_2$	$2\nu_2$		$5\nu_1$	$3\nu_1 + \nu_2$	$\nu_1 + 2\nu_2$	$6\nu_1$		$2\nu_1 + 2\nu_2$	

These long shifts are nearly completely suppressed in 3 *N* salt solutions. These changes are also analogous to that of the 3233 band and were attributed to variations in the degree of association.

The Raman shift for water at $\Delta\bar{\nu}$ 1705 and 3474 was noted by Kimura and Uchida (128).

Bolla (162), with long exposures and excitation by the 2536 A.U. mercury line, observed nine or ten diffuse components in the water bands.

Rafalowski (179) observed a sharpening of the water band with increasing concentration of nitric acid. With hydrochloric acid the intensity of both outer components decreases with increased concentration while the middle component is broadened.

Hatley and Callihan (168) obtained a water band consisting of three components. The effects on this band of various concentrations of aqueous solutions of potassium chloride, sodium hydroxide, and potassium hydroxide are to cause the tops of the curves to grow sharper with increasing concentration and the energy to shift to the long wave length side (increased λ).

Specchia (185, 186) stated that the water band consists of three components. The effect of temperature is to decrease the intensity of the three components with increasing temperature and to cause a slight displacement towards the lower frequencies of the maxima.

Hibben (125) has pointed out that as the concentration of aluminum chloride or zinc chloride in solution is increased the water band becomes more intense and much sharper, with the maximum at $\Delta\bar{\nu}$ 3418 for the central band. Nisi (176) found two bands for water—$\Delta\bar{\nu}$ 3135 and 3437. Notwithstanding this, the water band—excited by the 4047 A.U. and 3650 A.U. mercury lines—apparently looked like triplets. At temperatures of 100°C. there is not much difference in structure except that the lower frequency shift fades somewhat.

True water of crystallization shows three bands much sharper than those in liquid water. These (138) are $\Delta\bar{\nu}$ 3230, 3400, 3500. Nisi (176) studied the Raman bands due to crystallization in a number of sulfate salts. Most of these show but one band, namely, at approximately $\Delta\bar{\nu}$ 3400. Others such as the pentahydrate of copper sulfate show three bands at $\Delta\bar{\nu}$ 3211, 3377, and 3494, all of which are somewhat sharper than in the case of liquid water. The intensities of the bands in some hydrates such as gypsum vary somewhat, depending upon the direction of observation and illumination of the crystal.

It is difficult to evaluate these results since they are so discordant. It seems probable that some of these differences may be rightfully attributed to differences in degree of polymerization of the water examined. It is also probable that a contributing factor is the misinterpretation of spurious lines as suggested by Hulubei. It is also to be admitted that no accurate evaluation of the maxima can be reached except by microphotometric means, which have not always been employed. Notwithstanding these allowances, there still remain some unexplained discrepancies. Some observers find only two bands. The preponderance of evidence, however, is in favor of at least three of the higher frequency components. The behavior with temperature is also a matter of question, with the evidence approximately equally divided between an increase and a decrease in the $\Delta\bar{\nu}$ 3590 band. Presumably, however, the 3220 band decreases in intensity with increased temperature. It is a fact that the addition of electrolytes to aqueous solutions profoundly modifies the general character of the water band, particularly with increased concentration.

It is, furthermore, possible that this modification may be somewhat different with different types of electrolytes. This modification of symmetry is also equally apparent in the water of crystallization. How this may change with temperature is as yet undetermined, as is the number of water bands to be expected. The existence of low frequency oscillations, as noted by Segré and also by Bolla, $\Delta\bar{\nu}$ 60, 140 (172), is of considerable interest if they can be definitely shown to be due to the oscillation of water polymers. The large frequency shifts observed by Hulubei are consistent with the infra-red absorption spectra but have not been noted by other observers.

The essential fact brought out in these investigations is the anomalous behavior of water under different conditions of temperature and of electric environment (containing a solute). This has been most logically explained on the basis of changes in the molecular aggregations of which water consists, and is compatible with similar conclusions derived from other physico-chemical evidence.

VI. The Raman Effect in Acids and Bases

One of the most fruitful applications of the Raman effect is in the investigation of the constitution of acid solutions of varying concentrations. While conductivity measurements and determinations of hydrogen-ion concentrations by various methods have given a picture of the stepwise dissociation of polybasic acids as well as the fraction of undissociated molecules remaining in solution, practically no such method has any meaning in solutions of high concentration. The Raman method, on the contrary, can be applied to solutions from 100 per cent acid to those of a few per cent. Not only is it possible to follow a normal dissociation phenomenon, but it is also possible to distinguish and identify the appearance of other molecular species which may be coëxistent. These data are obtained from the following consideration. In the experiment, if the exposure time is increased in proportion to dilution, the intensity of the Raman lines characteristic of the substance examined will remain constant, provided there is no intervention of another factor. If, however, dilution or concentration under these conditions causes a change in the molecular configuration or constitution of the acid, there will result a corresponding anomalous Raman effect.

Nitric acid

Such a system has been investigated by Rao (213, 214). Nitric acid was studied in concentrations ranging from 65 per cent acid to 9.7 per cent. The most concentrated acid yielded $\Delta\bar{\nu}$ 1299, 1110, 1046, 957, 685, 638. Of these $\Delta\bar{\nu}$ 638, 685, and 1046 were attributed to the nitrate ion. The remainder, $\Delta\bar{\nu}$ 957, 1110, and 1299, were attributed to the undissociated nitric acid molecule. In addition, $\Delta\bar{\nu}$ 3202, 3427, and 3439–3525, belonging to water were observed. A fourth long-frequency shift, $\Delta\bar{\nu}$ 3321, was also attributed to the undissociated acid. The results are given in figure 12. In this figure the horizontal line at the top of each curve represents complete blackening of the photographic plate. The maxima, marked with a downward arrow, correspond to the undissociated HNO_3 molecules, their intensity diminishing so rapidly that they are almost extinct in the fourth curve, corresponding to a concentration of 39 per cent. The maxima, denoted by an upward arrow, are for the nitrate ion lines, which very rapidly increase in intensity up to 39 per cent concentration. These then diminish again, showing that on initial dilution the dissociation increases much more rapidly than the diminution in concentration, but after a certain stage the dissociation increase becomes less in proportion to diminution in concentration of the ions. It can also be seen that the intensity of the continuous spectrum increases with dilution.

From the relative intensities of the lines ascribed to nitrate ions it is possible to calculate the degree of dissociation and compare it with that obtained by other methods, namely, conductivity and viscosity. This is given in figure 13, in which the lowest curve has been obtained from viscosity–conductivity data, the middle from Kohlrausch's conductivity formula, and the upper from measurements of Raman lines for the nitrate ion. The departures from the Raman method curve are ascribed by Rao to the inapplicability of standard methods to measure the true degree of dissociation even at moderate concentrations.

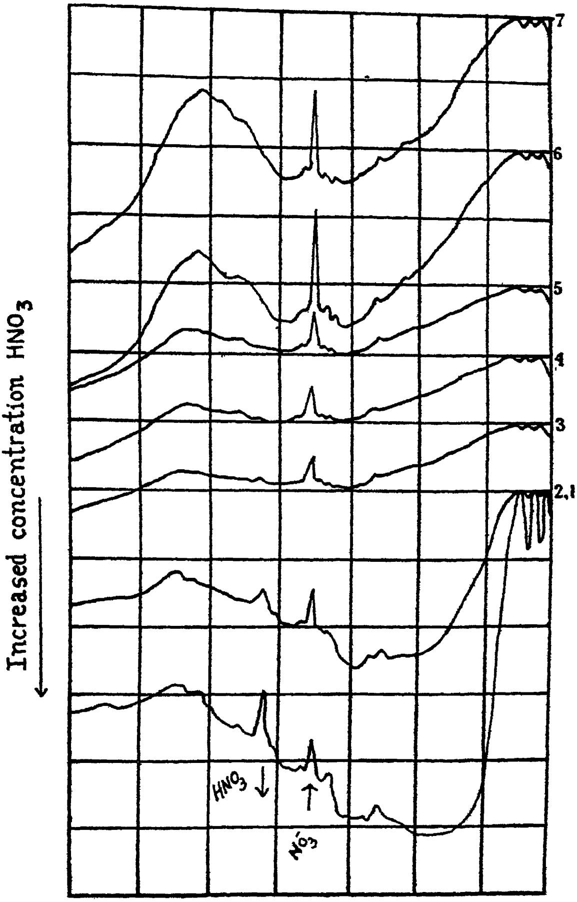


FIG. 12. CHANGES IN THE CHARACTERISTIC RAMAN FREQUENCIES OF NITRIC ACID WITH VARYING CONCENTRATION

Showing increase in nitrate ions and decrease in nitric acid molecules with dilution (after Rao).

The picture, however, is not quite so simple as has just been painted. Kinsey (204) finds in nitric acid solutions, with the exception of $\Delta\bar{\nu}$ 3321 and $\Delta\bar{\nu}$ 1110, approximately the same lines as observed by Rao. These wave number shifts are $\Delta\bar{\nu}$ 618, 669, 937, 1034, and 1293. Of these, $\Delta\bar{\nu}$ 618 and 669 (Rao's $\Delta\bar{\nu}$ 630 and 689) behaved in exactly the same manner as $\Delta\bar{\nu}$ 937 and 1293, disappearing completely in a 25 per cent solution. This, then, is tacitly attributing the first two of these lines not to the nitrate ion but to the HNO_3 molecule. The 3321 shift noticed by Rao is attributed to excitation by 3650 A.U. mercury line and would correspond to a shift between $\Delta\bar{\nu}$ 618 and 669 if this were the source of the excitation.

Concentration %

FIG. 13. DEGREE OF DISSOCIATION OF NITRIC ACID AS DETERMINED BY THE RAMAN EFFECT

Curve 1 represents the degree of dissociation as determined from the intensity of the nitrate ion lines, curve 2 the dissociation from conductivity measurements, and curve 3 the dissociation from viscosity–conductivity measurements (after Rao).

Woodward (223, 225) investigated quantitatively the behavior of concentrated nitric acid solutions on dilution. An anomaly revealed by the Raman spectrum was also observed by him. His interpretation, however, differs slightly from that of his predecessors. Solutions containing 14 moles, 9.6 moles, 5.2 moles, and 1.5 moles of nitric acid per liter were examined. The 14 molar solution yields $\Delta\bar{\nu}$ 1311 strong, 1048 very strong, 961 medium, 697 weak, and 643 weak. The line corresponding to $\Delta\bar{\nu}$

1048 was attributed to the nitrate ion. $\Delta\bar{\nu}$ 1311, 961, 697, and 643 are attributed by Woodward to undissociated nitric acid. These increase in intensity with increase of the concentration. At the same time there is a decrease in the $\Delta\bar{\nu}$ 1048 associated with the nitrate ion. In principle this is much the same result as obtained by Rao and Kinsey. Woodward likewise does not find $\Delta\bar{\nu}$ 3321. The change in ionization was further found not to be a function of temperature, since the lines did not change in intensity with experiments carried out at 5°C. and 75°C. The Raman spectrum of nitric acid molecules is more nearly similar to that of nitrate crystals than to the free ion.

Dadieu and Kohlrausch (194) have investigated the Raman spectra of highly concentrated nitric acid solutions with particular reference to the constitutional form of nitric acid From an examination of organic and inorganic nitrites and nitrates they conclude that the internal oscillations of the nitro group have the following frequencies,

$Ar \cdot NO_2$	$\Delta\bar{\nu}_1 = 1520$,	$\Delta\bar{\nu}_2 = 1340$
$R \cdot NO_2$	$\Delta\bar{\nu}_1 = 1560$,	$\Delta\bar{\nu}_2 = 1380$
$R \cdot O \cdot NO_2$	$\Delta\bar{\nu}_1 = 1627$,	$\Delta\bar{\nu}_2 = 1274$

in which $\Delta\bar{\nu}_2$ is the more intense. This leads to the conclusion that $\Delta\bar{\nu}$ 1300, found in the nitric acid solutions, can be explained by the fact that a not inconsiderable portion of the dissolved nitric acid assumes the formula $HO \cdot NO_2$. However, if this is the case, it must be first demonstrated that a second frequency at about $\Delta\bar{\nu}$ 1625, also known to belong to the NO_2 group, is present, and last, that the spectrum of nitric acid with increasing concentration must approach near to the type of spectrum found in the organic nitrate $R \cdot O \cdot NO_2$. The results are given in table 6.

The $\Delta\bar{\nu}$ 1038 is attributed to the nitrate ion. The appearance of $\Delta\bar{\nu}$ 1665 and 1687 is confirmatory of the existence of the ester or pseudo-acid form of nitric acid. Frequencies corresponding to C—H oscillations are omitted in the table. The line corresponding to $\Delta\bar{\nu}$ 3420 would be attributed to the homopolar O—H binding, but is considered uncertain.

A similar line of reasoning has been given by Brunetti and Ollano (191, 192). They assume that one may have an equilibrium in the acid solution as given by Hantzsch (200).

$$NO(OH)_2(NO_3) \rightleftarrows 2O_2N \cdot OH$$

On this theory, by adding water one obtains the hydrate of the pseudo-acid $O_2N \cdot OH \ldots H_2O$, salts of the hydroxonium type, $(NO_3)H_3O$, salts of the polyhydroxonium type, $(NO_3)(H(H_2O)_n)$, and hydrates of the ions of this salt, $(NO_3)(H_2O)^-$ and $(H(H_2O)_n)^+$.

TABLE 6

Concentrated nitric acid and organic nitrates

I HNO_3 (64 per cent)	II HNO_3 (100 per cent)	III $H_3C \cdot O \cdot NO_2$
—	—	353
635	607	580
684	667	663
949	916	860
—	—	994
1038	—	—
—	—	1170
1302	1292	1276
1625	1665	1630
1668	1687	
—	[3420]	—

Hence radiation should be found due to the NO_2 and NO_3 groups and to NO_3 ions and H_3O ions. To the NO_2 group were ascribed the frequencies $\Delta\bar{\nu}$ 815, 1241, and 1236. To the NO_3 ions were ascribed $\Delta\bar{\nu}$ 717, 1049, and 1389. Concentrated nitric acid solutions were next examined in concentrations varying from 13.4 moles to 2.7 moles in eight steps.

The results of Brunetti and Ollano may be summarized as follows: all nitric acid solutions exhibit $\Delta\bar{\nu}$ 1045 and 1395, weak in the dilute solutions. At less than 10 molar there is also present $\Delta\bar{\nu}$ 716, all these frequency shifts being in common with the nitrates. The frequencies characteristic of the NO_3 group diminish in intensity as the solution becomes less concentrated in nitrate ions.

In the more concentrated solutions other frequencies are noted, particularly one at $\Delta\bar{\nu}$ 1306, similar in aspect to $\Delta\bar{\nu}$ 1326 in the nitrites but certainly displaced about twenty wave numbers. However, when this line is most intense, $\Delta\bar{\nu}$ 815 and 1240, characteristic of the nitrites, are not present. Furthermore, $\Delta\bar{\nu}$ 1306 (NO_2) disappears at concentrations of 7 molar or approximately 25 per cent.

In addition to the frequencies cited, $\Delta\bar{\nu}$ 640, 690, and 950 are also obtained, intense in concentrated solutions and disappearing on dilution. In 65 per cent nitric acid and somewhat less, $\Delta\bar{\nu}$ 1138 was also observed. Brunetti and Ollano concluded that the presence of the frequency $\Delta\bar{\nu}$ 1306, together with a strong water band at $\Delta\bar{\nu}$ 3589, justifies the opinion that there exists in aqueous nitric acid not only $O_2N \cdot OH$ but also an aggregate of the form $O_2N \cdot OH \cdot H_2O$. The value of the concentration at which the NO_2 frequency disappears (under 7 molar) is in accord with the calculations of Hantzsch (201). In concentrated solutions, therefore, the nitrate ions do not manifest themselves as such but rather as NO_2 groups.

The foregoing discussion represents the more recent developments in the determination of the constitution of nitric acid. It is certain that the factual data demonstrate the existence of an anomalous behavior. It is equally certain that the Raman effect method is one of the most logical means of investigating this behavior. It is probable that most of the conclusions drawn are in accordance with facts. The Raman effect evidence probably gives a fairly close picture of the actual ionization process. It is also probable that the formula HNO_3 does not represent the true constitution of nitric acid. It is more than possible that in higher concentrations the acid is more accurately represented by the formula $HO \cdot NO_2$. What divergent results there are in these experiments are mainly due to ambiguous interpretations and to the failure to use a proper monochromatic source of radiation. The overlapping of the water bands has added not a little to the confusion. While the constitution proposed by Hantzsch and adopted by Brunetti and Ollano may have considerable foundation, the actual experimental results provide little or no data upon which the existence of H_3O^+ and salts of the polyhydroxonium type may be predicated.

Sulfuric acid

The first Raman investigations of sulfuric acid were more concerned with the number of Raman lines obtainable than with any anomalous effects to be observed with dilution (155, 167, 219, 221).

Some of these early investigators reported wave-number shifts between approximately $\Delta\bar{\nu}$ 2000 and $\Delta\bar{\nu}$ 2300. These are probably erroneous. Later, more accurate determinations at different concentrations were made. Nisi (208) obtained at least seven characteristic fairly strong Raman bands, for example, in 10 per cent solutions, $\Delta\bar{\nu}$ 432, 598, 893, 978, 1046, and 1200. A 75 per cent solution gave $\Delta\bar{\nu}$ 417, 578, 913, 1035, 1167, and 1313. Pure H_2SO_4 gave $\Delta\bar{\nu}$ 414, 564, 740, 911, 1043, 1170, 1366, 1517. Of these $\Delta\bar{\nu}$ 911 is the strongest in the concentrated state, but the intensity of this band and the continuous background spectrum gradually fall off with dilution. This is attributable to H_2SO_4 molecules. The band of about $\Delta\bar{\nu}$ 1040 becomes strong rapidly with addition of a small quantity of water. The band of $\Delta\bar{\nu}$ 980 begins to appear only when the acid is diluted to approximately 50 per cent, and increases with dilution. These two bands, viz., 980 and 1040, are attributed to the $SO_4^{=}$ and HSO_4^- groups, respectively. The diffuse bands $\Delta\bar{\nu}$ 1170, 564, and 414 increase slightly in wave-number shift with decrease in concentration. These three bands appear frequently in sulfate solutions. The band at $\Delta\bar{\nu}$ 1366 appears only in concentrated solutions.

Woodward (223, 225) has also quantitatively examined the Raman spectrum of sulfuric acid as a function of concentration. These experiments were carried out in a more quantitative fashion, since exposure was made proportional to the dilution. A similar anomalous behavior was observed. For a 10 per cent solution he obtained $\Delta\bar{\nu}$ 437, 613, 985, 1048, and 1205; for 75 per cent, $\Delta\bar{\nu}$ 432, 588, 912, 1043, and 1163; for 100 per cent, $\Delta\bar{\nu}$ 400, 560, 908, 1143, and 1359. With decreasing acid concentration there is an increase in the intensity of $\Delta\bar{\nu}$ 1048. At the same time there is a marked decrease in $\Delta\bar{\nu}$ 908, the strongest line of the pure acid. In acids of medium concentration, that is, approximately 25 to 50 per cent, there appears a line $\Delta\bar{\nu}$ 982 not present in the more concentrated solutions. This increases in intensity with dilution. These changes are depicted in figure 14, where curve I corresponds to 100 per cent, curve II to 90 per cent, curve III to 50 per cent, and curve IV to 25 per cent sulfuric acid. These alterations in intensity are reasonably explicable if one assumes that $\Delta\bar{\nu}$ 908 is associated with the H_2SO_4 molecule and hence decreases in intensity with increased dilution. This presupposes that the concentration of H_2SO_4, as such, decreases

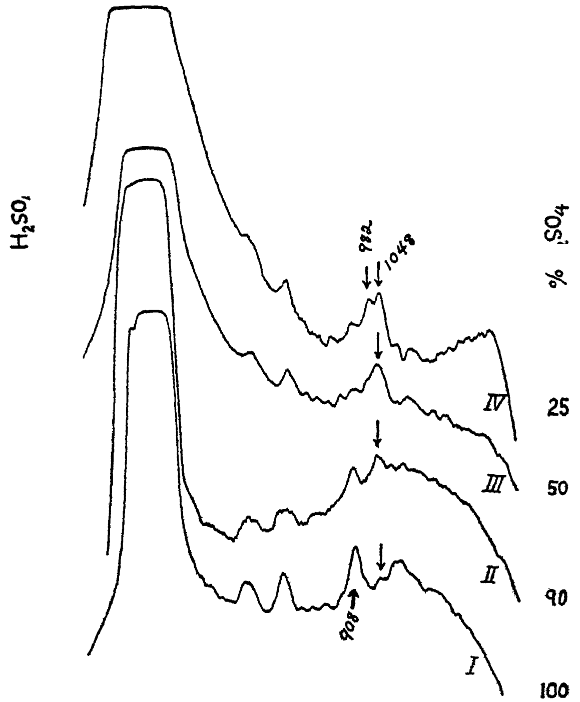


Fig. 14. Changes in the Characteristic Raman Frequencies of Sulfuric Acid with Varying Concentrations

$\Delta\bar{\nu}$ 908 characteristic of sulfuric acid molecule decreasing in intensity with dilution; $\Delta\bar{\nu}$ 1048 characteristic of HSO_4 ion, and $\Delta\bar{\nu}$ 982 characteristic of SO_4 ion increasing in intensity with dilution (after Woodward).

owing to ionization. On the other hand, $\Delta\bar{\nu}$ 1048, on the average, is associated with the HSO_4 ion. The production of HSO_4 ions as a first step in the ionization process would give an increase in intensity of this line with dilution. Furthermore, $\Delta\bar{\nu}$ 982 is presumed to be associated with the SO_4 ion. This appears only in fairly dilute solutions as a result of the dissociation of HSO_4 into SO_4 ions and hydrogen ions. This naturally likewise increases in intensity with dilution. This is somewhat confirmed by a study of the Raman spectrum of $KHSO_4$ which gives $\Delta\bar{\nu}$ 1056, 982, and 593, the former two being moderately strong. $\Delta\bar{\nu}$ 982 is present in all sulfates.

The line corresponding to the shift $\Delta\bar{\nu}$ 1048, presumably characteristic of the HSO_4 ion, is found to be moderately strong in the Raman spectra of pure acid as determined by Nisi, while completely absent in the observations of Woodward. The latter remarks, however, that the addition of only a small quantity of water to the pure acid evokes this line, and it is presumed that the acid used by Nisi contained small quantities of water.

Bell and Fredrickson (190) made somewhat similar observations. The $\Delta\bar{\nu}$ 1048 increases in intensity with dilution. The $\Delta\bar{\nu}$ below this value apparently decreases in intensity with dilution. At approximately 40 per cent, $\Delta\bar{\nu}$ 1200 appears and persists in dilute solutions. A change in the intensity of $\Delta\bar{\nu}$ 1048 is attributed, perhaps, to a hydrated hydrogen ion. The intensity variations, however, were estimated only by visual inspection.

Fadda (198) found that concentrated sulfuric acid shows none of the characteristic frequencies of the SO_4 group, but in all concentrations less than 25 per cent the spectrum shows $\Delta\bar{\nu}$ 984, which is the most intense in the sulfates.

The effect of an electric field on a 50 per cent solution of sulfuric acid was determined by Ricca (215). When the direction of the current is such that the hydrogen ions move toward the spectrograph, the higher frequency end of the bands is broadened. With the current in a reverse direction the shift is in the opposite direction.

Specchia (218) noted that in solutions of sulfuric acid there is a progressive displacement with dilution of the Raman lines toward greater wave lengths. A decrease in the intensity of $\Delta\bar{\nu}$ 892 and an increase in intensity of $\Delta\bar{\nu}$ 1052 were observed with dilution. At low concentrations of acid (13.5 per cent) no substantial modification in the essential characteristics of the Raman spectra of the acid was observed.

The results with sulfuric acid obtained by different observers are more concordant than those in the case of nitric acid. In the main, they point fairly clearly to the stepwise dissociation of sulfuric acid with dilution by means of the initial formation of HSO_4 ions and the latter's subsequent dissociation into SO_4 ions. The actual molecular constitution of the acid is still a nearly unknown entity. One thing is definite, however, namely, that the hydrogens in sulfuric acid are hydroxyl hydrogens, since the characteristic S—H shift is approximately 2600 wave numbers, a shift which is not present in any of these salt or acid solutions.

Sulfurous acid

The spectrum of sulfurous acid as measured is not completely different from that of sulfuric acid. An analysis of the results obtained by Fadda (198) gives a very interesting insight into the constitution of this acid. The $\Delta\bar{\nu}$ obtained were 569, 1047, 1142, and 1199, of which $\Delta\bar{\nu}$ 1142 was the most intense. These results were compared by Fadda with the $\Delta\bar{\nu}$ obtained from sulfates, acid sulfates, and sulfites. These are given in table 7.

It is immediately apparent that there is no common likeness between the spectrum from sulfurous acid and that from sodium sulfite or sodium sulfate. Two shifts, namely, $\Delta\bar{\nu}$ 569 and $\Delta\bar{\nu}$ 1047, are similar to those obtained in the acid sulfates. The presence of these lines was therefore attributed to the oxidation of a part of the sulfurous acid to sulfuric. The $\Delta\bar{\nu}$ 574 in sulfuric acid is not a constant value but changes slightly in frequency from $\Delta\bar{\nu}$ 561 for a 100 per cent solution to $\Delta\bar{\nu}$ 613 in a 10 per cent solution. $\Delta\bar{\nu}$ 569, therefore, falls within the range of $\Delta\bar{\nu}$ given by HSO_4 ions as determined from the Raman spectra of sulfuric acid. Most significant is the shift $\Delta\bar{\nu}$ 1142. This frequency is the characteristic one for sulfur dioxide (111, 202, 197, 209). $\Delta\bar{\nu}$ 1199 can perhaps be attributed to a shift characteristic of an

HSO_3 ion, but this is incapable as yet of direct substantiation. The absence of a line corresponding to approximately $\Delta\bar{\nu}$ 450 is without other explanation than an intensity factor.

For sulfurous acid Nisi (209) observed $\Delta\bar{\nu}$ 427, 528, 1017, 1054, 1152 and 1337, of which $\Delta\bar{\nu}$ 1337 was considered very strong. $\Delta\bar{\nu}$ 1054 was attributed to the HSO_3 ion.

The summary conclusion from these data, therefore, is that, on the whole, sulfurous acid does not exist as such in solution, but, on the contrary, retains the characteristics of sulfur dioxide except for a fraction which may be oxidized by atmospheric oxygen to form sulfuric acid. This is consistent with conclusions already drawn from infra-red absorption investigations (217).

TABLE 7

Sulfates, sulfites, acid sulfates, and sulfurous and sulfuric acids

Na_2SO_3	Na_2SO_4	$KHSO_4$	H_2SO_3	H_2SO_4*
471	460	427	569	421
602	617	593	1047	574
984	984	978	1142	985
—	1104	1047	1199	1047

* Incomplete.

Hydrochloric and other halogen acids

The Raman spectrum of hydrochloric acid has been investigated as a function of concentration (167). There are no lines attributable to HCl, but a marked decrease was noted in the width of the water band with the increasing concentration of hydrochloric acid. Other observers (116, 196) have found no Raman lines in hydrochloric acid solutions, although $\Delta\bar{\nu}$ 2885 has been observed for gaseous hydrogen chloride (222) and $\Delta\bar{\nu}$ 2781 for liquid HCl (216). These results are to be expected if the HCl is completely ionized in solution. In both the liquid and gaseous states the binding is homopolar and would consequently give rise to a value corresponding to the linear vibrations of hydrogen–chlorine.

Woodward (223, 225) reinvestigated the Raman spectrum of hydrochloric acid in concentrated aqueous solution and in organic solvents, such as benzene, xylene, and carbon tetrachloride, but could find no evidence of any associated hydrochloric acids.

He also investigated the Raman spectrum of hydrofluoric acid (40 per cent). It is well-known that this acid is polymerized in the vapor phase, and conductivity measurements would indicate the presence of an HF_2 ion from the dissociation of H_2F_2 (195, 188). No Raman lines were observed. However, a strong continuous background spectrum is present which tends to mask any weak Raman lines. In spite of this fact, it is surprising that no lines were elicited if hydrofluoric acid has the constitution generally attributed to it. It is probable that this material will be reinvestigated and this point clarified.

Other inorganic acids, such as iodic acid (134, 208, 196, 225, 223) and perchloric acid (208, 210, 219) have been investigated. Krishnamurti found for iodic acid $\Delta\bar{\nu}$ 327, 633, 713, 781, the last three $\Delta\bar{\nu}$ being designated as strong. Nisi observed in a weak solution $\Delta\bar{\nu}$ 317, 393, 799, 805, the first two $\Delta\bar{\nu}$ being weak, $\Delta\bar{\nu}$ 799 medium, and $\Delta\bar{\nu}$ 805 strong. Woodward (225) obtained $\Delta\bar{\nu}$ 335, 649, 796, the last two being strong, the other one medium. Dickinson and Dillon (196) obtained $\Delta\bar{\nu}$ 800 strong and $\Delta\bar{\nu}$ 329 medium in a 45 per cent solution. There are some discrepancies in these results, but none of the experiments were carried out under comparable conditions. The absence of a line at $\Delta\bar{\nu}$ 649 in the dilute solutions may or may not have some significance. It is presumed by Woodward that in 10 N solutions the iodic acid is completely dissociated. A thirty per cent solution of perchloric acid gave the following lines according to Nisi: $\Delta\bar{\nu}$ 464, 628, 932, 1115, $\Delta\bar{\nu}$ 932 being strong and the remainder of medium intensity. These results are confirmed by Ollano (177), who obtained $\Delta\bar{\nu}$ 461, 627, 936, and 1118 for the ClO_4 ion in perchloric acid (6 moles per liter), by Dickinson and Dillon (196), who obtained $\Delta\bar{\nu}$ 470, 634, and 935 (strong) in a 60 per cent solution, and by Taylor (219). A strong, wide band appearing at $\Delta\bar{\nu}$ 3550 and a weaker band at 3590 were ascribed by Ollano to hydroxonium $(H_3O)^+$ and polyhydroxonium $(H(H_2O)_n)^+$ ions, respectively. As has been mentioned in the discussion of the Raman spectra of water, the latter conclusion is to be accepted with caution. This becomes still more evident after consideration of the Raman spectra of hydroxides. That acids, salts, and alkalies have an influence on the water band is undoubted, but the attributing of an ill-defined band to a particular homopolar linkage without statistical data as to the origin of that particular frequency, and without other supplementary evidence, is actually extrapolating beyond the experimental information given.

Selenic acid is presumed by Pringsheim and Yost (212) to have some similarity in structure to sulfur trioxide. It gives $\Delta\bar{\nu}$ 695–885.

Phosphoric and phosphorous acids

Solutions containing 25, 50, and 84 per cent phosphoric acid were examined by Nisi (208). He obtained $\Delta\bar{\nu}$ 356, 498, and 911 in the highest concentration, $\Delta\bar{\nu}$ 512, 906 in the medium concentration, and $\Delta\bar{\nu}$ 505, 898 in the more dilute solution. The largest wave-number shift was the strongest, the others medium and diffuse. It is quite uncertain whether the change in $\Delta\bar{\nu}$ with concentration has any real significance. It was suggested that the lines owe their origin to the H_2PO_4 group.

The Raman spectrum of phosphorous acid has been determined by Ghosh and Das (199). The $\Delta\bar{\nu}$ obtained were 672, 940, and 1012, the 940 being the strongest. The lines were attributed to an H_2PO_3 ion. Neither of these acids has been very carefully investigated. The lines are somewhat broad, and in concentrated solutions there is a strong continuous spectrum (124).

Hydrolysis of acid salts

Krishnamurti (205) has investigated the hydrolysis of salts into the free base and free acid. There are three possibilities: namely, hydrolysis of (a) weak bases and strong acids, (b) weak acids and strong bases, (c) weak acids and weak bases. It is necessary to choose a case where the degree of hydrolysis is fairly large and where the molecule of the base or acid has at least one strong line different from that of the salt. It was found that the case of a weak base and strong acid is most favorable. Urea hydrochloride in concentrated aqueous solution gives one strong line at $\Delta\bar{\nu}$ 1016 and two weak lines at $\Delta\bar{\nu}$ 513 and 578. Urea itself gives one strong line at $\Delta\bar{\nu}$ 999 and two weak lines at $\Delta\bar{\nu}$ 533 and 1158. In a 4 N solution of the salt the same lines persist as for concentrated urea hydrochloride, but on further dilution $\Delta\bar{\nu}$ 999 appears and increases in intensity until it is approximately equal to that of $\Delta\bar{\nu}$ 1016. This appearance of the strong line characteristic of urea is attributed to the progressive hydrolysis of the salt.

Raman spectra of hydroxides

Krishnamurti (96) observed the Raman spectra of sodium, strontium, and barium hydroxides. Of these only sodium hydroxide gave a line which could be ascribed with any degree of certainty to the hydroxide group. This shift is $\Delta\bar{\nu}$ 3630. Woodward (224) obtained in 10 to 12 N sodium and potassium hydroxide solutions $\Delta\bar{\nu}$ 3615, together with a strong continuous spectrum also observed by Bär (189). This line is broad and diffuse and comparable with the value $\Delta\bar{\nu}$ 3603 observed by Nielsen (207) and also by Thompson and Nielsen (220).

The magnitude of this shift is of the same order as that attributed to the $H \longleftrightarrow O$ vibration by $\Delta\bar{\nu}$ 3388 in methyl alcohol (193) and $\Delta\bar{\nu}$ 3420 for the $H \longleftrightarrow O$ vibration in ethyl alcohol (203). Nielsen has pointed out that if one assumes the vibration frequencies can be expressed by the formula given by Mecke (206), two vibration frequencies are obtained which do not deviate much from each other. He concludes that it is not improbable that $\Delta\bar{\nu}$ 3603 belongs to OH ions and that the great width of the ordinary water band is related to the hydration of these ions in water. The effect of increased concentration of sodium hydroxide is shown in figure 15.

Hatley and Callihan (168) obtained three bands for water, namely, $\Delta\bar{\nu}$ 3228, 3435, 3624, and studied the displacement of these bands as a function of sodium and potassium hydroxide concentrations, varying between approximately 1 N and slightly greater than 10 N. It was observed in both cases that with increased concentration the center of gravity of the water band shifted towards higher frequency, that is, $\Delta\bar{\nu}$ 3624, which became much stronger with increasing concentration of alkali, the inference being that the water and hydroxyl bands are practically identical, particularly with reference to the highest band observed for water.

It has been tentatively suggested by Carrelli, Pringsheim, and Rosen (116) that one of the lines observed in ammonium hydroxide solution ($\Delta\bar{\nu}$ 3385) might be attributed to the OH ion. Woodward contends that it is more likely that this frequency would be attributed to an undissociated OH group rather than the ion. This explanation, however, does not seem very plausible, since if this were the origin there should also be a reasonably strong frequency corresponding to the N⟷OH vibration in undissociated ammonium hydroxide as well as H ⟷ O in the same group. This latter argument is somewhat substantiated by the fact that hydroxylamine hydrochloride shows such a frequency (89) at $\Delta\bar{\nu}$ 995.

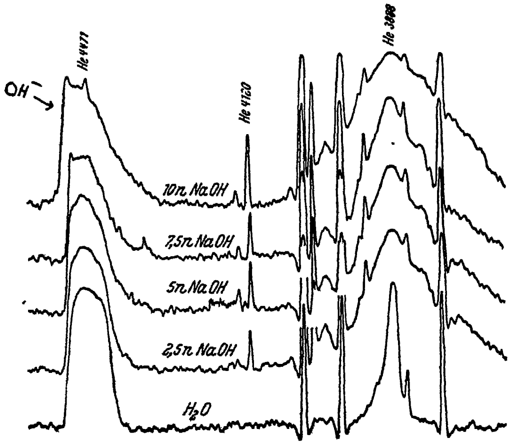
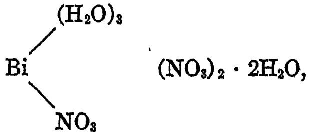
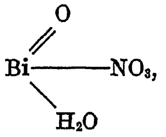


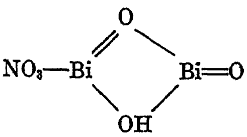
FIG. 15. RAMAN BANDS FOR WATER AND OH IONS WITH VARYING CONCENTRATIONS OF SODIUM HYDROXIDE

Showing persistence of OH band in concentrated solutions of sodium hydroxide (after Nielsen).

It is presumed by Ollano (24) that bismuth nitrate hydrolyzes in the presence of nitric acid to compounds to which he assigns the following structures:







The nitrate ion is in part ionized and in part attached directly to bismuth. It is postulated that aqueous nitric acid solutions of bismuth nitrate contain NO_3^-, Bi^{+++}, $BiOH^{++}$, and $Bi(OH)_2^+$. With diminishing concentration of the acid the concentration of the bismuth ions and $BiOH^{++}$ decreases, while that of $Bi(OH)_2^{++}$ increases. The spectrograms give in addition to the lines attributable to the nitrate ions $\Delta\bar{\nu}$ 3595, 1600, and 1500. Of these shifts, $\Delta\bar{\nu}$ 1600 at the lower concentrations has medium intensity, and $\Delta\bar{\nu}$ 1500 always appears intense and sharp. The last two frequencies are assigned to $Bi(OH)_2^+$ and $BiOH^{++}$ groups, respectively. The frequency $\Delta\bar{\nu}$ 3595 is assigned to the $H \longleftrightarrow O$ vibration. $\Delta\bar{\nu}$ 1236 is without assignment.

These allocations of wave-number shifts to specific molecular structure are admittedly somewhat arbitrary in view of the scant experimental data upon which they are predicated.

VII. THE RAMAN SPECTRA OF SOLUTIONS

The Raman spectra method of investigation, when applied to solutions, provides considerable information in regard to the molecular constitution of such systems. It is in no wise unreasonable to expect the same general type of spectrum to be elicited from a solute as would be obtained from its crystalline state of aggregation. The carbonate ion, for example, exists as such in the crystalline state and in solution, and consequently has a similar spectrum. In general, there are, however, certain pertinent differences: namely, the lines corresponding to lattice vibrations are totally absent in the solute, as is to be expected if the dissolved compound is ionized to any reasonable extent; the influence of the cation should be considerably less in solution for similar reasons; and complex ion or complex-compound formation in solution will result in definite anomalies. Polyatomic ionic groups may be treated, as a first approximation, in the same manner as a gas consisting of the same number of atoms arranged in the same type of spacial configuration. The effect of the solute on the Raman spectrum of the solvent is by no means insignificant, as has been discussed in the Raman spectra of water. The rôle played by the solvents and its influence on the Raman spectrum of the solute due to changing electrical environment are likewise frequently not entirely negligible.

As a preliminary to the discussion, the Raman spectra obtained from most of the inorganic solutions so far studied are given in tables 8 to 16. The spectra obtained from carbon and nitrogen compounds and inorganic complexes will receive special treatment. In these tables some of the relative intensities are indicated by the subscripts s, m, and w, denoting strong, medium, and weak. In most cases these are visual estimates. Where no indications are given, either no estimates were available or the intensities were faint. When only one shift is recorded this is probably the most intense one. It is obvious that there is some divergence in opinion in regard to the weaker lines, particularly when those lines are rather broad. The absence of the proper number of Raman lines for a given configuration is probably indicative of a failure to elicit these lines rather than their actual absence. The wave-number shifts enclosed in parentheses are somewhat doubtful and those followed by a question mark are very doubtful.

A. TYPE AO_2

In examples where the number of Raman lines equal or exceed the minimum requirement, there may be some real differences of opinion, for example in the case of sodium nitrite, where Brunetti and Ollano (191) differ from Carrelli, Pringsheim, and Rosen (116), both as to the magnitude of the shifts and their number.

In general, molecules of the type containing a non-linear triatomic ion should give three fundamental oscillations. This number may be exceeded owing to degeneracy, to combination frequencies, or to other causes. In any case these lines will be much weaker than the fundamentals. In this type of molecule

TABLE 8

Inorganic solutions (*type* XO_2)

SUBSTANCE	CONCENTRATION	RAMAN SHIFTS*											REFERENCES
$NaNO_2$			588_w	655	715	814_w			1220	1324_s			(231)
$NaNO_2$	Saturated			696_w		785				1303_s		2151?	(116)
$NaNO_2$						815			1241	1326_s			(191)
KNO_2			596	658_w	710	816			1208	1321_s			(231)
$Ca(NO_2)_2$			596	663_w	714	825			1231	1327_s			(231)
$Ba(NO_2)_2$			592	649_w	710	811				1325_s			(231)
$NaBO_2$		253									1403_m		(199)
NaH_2PO_2							952	1080_w					(199)
H_2O_2						875_s	903						(259)

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* The relative intensities are indicated by subscript letters following the numerical values of the Raman shifts: s = strong, m = medium, w = weak. The lack of any such designation indicates either that the line is faint or that there are no comparative data available in regard to the intensities. When the compound has been investigated by more than one observer, the shifts given do not usually represent the average value, but are preferentially selected from the more exact experimental determinations. In the case of considerable disagreement among observers the differing Raman shifts are generally included in parentheses.

TABLE 9

Inorganic solutions (*type* XO_3)

SUBSTANCE	CONCENTRATION	RAMAN SHIFTS*											REFERENCES
$NaClO_3$	51 per cent				479_w	611			932_m				(196)
$Mg(ClO_3)_2$	Saturated			376?	533	604			930_m				(254, 256)
$NaBrO_3$	26 per cent			367_w				810_m					(196)
KIO_3								806					(208)
$KHSeO_3$				339				852					(212)
H_2SeO_3							695	885					(212)
Na_3AsO_3		144	203										(199)
$NaVO_3$			228	367									(199)
$NaPO_3$												1137	(199)
NaH_2PO_3						642_s			925		1068_s		(199)
Na_2HPO_3								893		980	1030		(199)

* See footnote to table 8.

the shift at $\Delta\bar{\nu}$ 1325 in the case of nitrites is an inactive frequency due to symmetrical vibrations. Ghosh and Das (199) have attributed $\Delta\bar{\nu}$ 1403 for $NaBO_2$ and $\Delta\bar{\nu}$ 1080 for $P(OH)_2$ also to this type of vibration. In both the latter instances, however, the third fundamental was not obtainable. The frequency shifts, however, increase in proportion to the increased mass of the central atom in the order, boron, nitrogen, phosphorus. While hydrogen peroxide is not a molecule of this type, the appearance of a strong line at $\Delta\bar{\nu}$ 875 is indicative of the oscillation of the two oxygens against each other, differing widely from the $O \leftrightarrow O$ vibration in O_2. This has not been studied sufficiently, however, to permit forming a definite opinion regarding the linearity or nonlinearity of the molecule.

B. TYPE XO_3

Krishnamurti (134) considers that for the crystalline chlorates, iodates, and bromates the molecular configuration is somewhat similar to that ascribed to ammonia by Dennison (26). This molecule was considered as a symmetrical tetrahedron with nitrogen at the apex. All four frequencies in the case of chlorates, bromates, and iodates are active. The intensities of the lines increase in the order of chlorine, bromine, and iodine. The strongest frequency is that which occurs between $\Delta\bar{\nu}$ 800 and 950, depending upon the compounds studied. This is attributed to the displacement of the central atom away from the plane of the oxygen atoms. The essential difference between the spectra from the crystals and those obtained from the solutions is that the strongest frequency shift in the case of a crystal is made up of several components, but in a solution gives a single broad line which represents an average of these values. The splitting up of this frequency shift into several parts in going from solution to crystal is essentially attributable to the distortion of the XO_3 group produced by the field of neighboring cations.

The Raman spectra studies with the remaining compounds given in table 9 are admittedly incomplete. There is, apparently, however, a real difference between the spectrum obtained from H_2SeO_3 and that from $KHSeO_3$ and among those compounds each of which contains a PO_3 group. So far as the evidence thus far obtained can be used as a criterion, the hydrogen in NaH_2PO_3 and Na_2HPO_3 cannot be linked directly to the phosphorus atoms. If this were the case, the line corresponding to this linkage would undoubtedly fall between $\Delta\bar{\nu}$ 2400 and $\Delta\bar{\nu}$ 2700. The characteristic H—S vibration in a solution of NaHS is $\Delta\bar{\nu}$ 2575. It is unlikely that a change from H—P to H—S would be of a different order of magnitude. By adding sodium hydroxide to a metavanadate solution, one can follow the progressive change of the metavanadate to the orthovanadate structure (199).

Nitrates

As has been previously stated, it is believed that the configuration of the nitrate ion is triangular, with the nitrogen in the center of the equilateral triangle. The most intense oscillation, $\Delta\bar{\nu}$ 1048, corresponds to the symmetrical expansion and contraction of the NO_3 group as a whole. Two other characteristic oscillations, $\Delta\bar{\nu}$ 726 and $\Delta\bar{\nu}$ 1357, are active vibrations. It was originally believed that these three frequencies in solution were independent of the cation and that the entire Raman spectrum was fairly simple (251). Subsequently, however, it has been observed by Grassmann (238, 239) and Nisi (148) that the intensity and magnitude of the shifts are a function both of the cation and the concentration of the solution. The frequency shifts obtained for various nitrates are given in table 10. Grassmann considers that $\Delta\bar{\nu}$ 720 to 730, which appear as a single line for the alkali nitrates, are split up into two components in calcium and cadmium nitrates, for example. In 8 *N* solutions these are of equal intensity. In 16 *N* solutions the $\Delta\bar{\nu}$ 741 line is stronger, and in 4 *N* solutions $\Delta\bar{\nu}$ 716 is the stronger. The shifts averaging $\Delta\bar{\nu}$ 720 are completely depolarized, while $\Delta\bar{\nu}$ 1048 is polarized. Nisi observed for the crystalline alkali nitrates a total change of 16 wave numbers proceeding from one end of the series to the other in the shift at approximately $\Delta\bar{\nu}$ 1048. There is a similar but much less pronounced change in the solutions of these salts, which would apparently indicate either an incomplete dissociation or an influence on the normal anion vibrations by the dissociated cations.

TABLE 10

Inorganic solutions (nitrates)

SUBSTANCE	CONCENTRATION	RAMAN SHIFTS*	REFERENCES
$LiNO_3$	14 *N*	1050_s	(120, 238, 239)
$NaNO_3$	33 per cent	721_w 1049_s 1361_w (1389) 1414 1663	(120, 251, 239, 196, 191, 148, 225, 164, 243, 257, 240, 116)
KNO_3	Saturated (20 per cent)	730_w 1049_s 1357_w 1413 1659	(251, 148, 243)
$RbNO_3$	20 per cent	1048_s	(148)
$CsNO_3$	20 per cent	1046_s	(148)
NH_4NO_3	64 per cent	728_w 1050_s 1332_w 1361 1400 1659	(116, 234, 196, 251, 255, 243, 148, 164)
$Cu(NO_3)_2$		279 442 717_m–754_w 1048_s 1325_w–1421 1476 1654	(184, 238)
$AgNO_3$		1041_s	(238, 239)
$Be(NO_3)_2$	3 *N*	1049_s	(258)
$CdNO_3$	8 *N*	716_w 741_w 1047_s	(238, 243, 239, 240)
$Mg(NO_3)_2$	3 *N*	(376) 1049_s 1346 – 1427 (1655) (1811)	(258, 254, 256)
$Ca(NO_3)_2$	Saturated	721 716_w–741_m 1050_s 1349 – 1441 1647 (1811)	(196, 251, 258, 238, 148, 184, 256, 239, 240)
$Sr(NO_3)_2$	Saturated	728_w 1049_s 1354_w	(251, 258)
$Ba(NO_3)_2$	Saturated	720_w 1049_s 1350_w	(251)
$Zn(NO_3)_2$	3 *N*	1047_s	(238, 258)
$Al(NO_3)_3$	3 *N*	1049_s	(258)
$Pb(NO_3)_2$	Saturated	730_w 1047_s	(251, 238, 239, 243)
$Bi(NO_3)_3$		730_w 980 1036_s (1236) 1417_w	(211)

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* See footnote to table 8.

This effect, however, is very close to the limit of accurate measurement of the wave-number shifts.

Silveira (184) also has observed a splitting in calcium nitrate of the $\Delta\bar{\nu}$ 720 shift to $\Delta\bar{\nu}$ 716 and 742, of which the latter is stronger. Similar behavior was observed in copper nitrate. In this case, however, $\Delta\bar{\nu}$ 717 was the more intense. There exists, furthermore, a second degeneracy of the average frequency, $\Delta\bar{\nu}$ 1357, in both of these compounds. This is split into two components, $\Delta\bar{\nu}$ 1325 and $\Delta\bar{\nu}$ 1421 for copper nitrate and $\Delta\bar{\nu}$ 1349 and $\Delta\bar{\nu}$ 1441 for calcium nitrate. No explanation is given for $\Delta\bar{\nu}$ 376 and 729. Silveira and Bauer (256) have observed a very feeble Raman shift at $\Delta\bar{\nu}$ 1811 for magnesium nitrate and calcium nitrate, for which there is equally no obvious explanation. The frequency shift at approximately $\Delta\bar{\nu}$ 1650 has been ascribed both to water (184) and to the nitrate ion (148). This band is very feeble and apparently appears in sulfate, chloride, or nitrate solutions. It is not, however, present in pure liquid water. Silveira and Bauer (256) attribute this band to a coupling between the ions and the molecules of water. This perturbation by water molecules is also held partially responsible for the doubling of the two degenerate frequencies of the nitrate ion. Unfortunately, however, $\Delta\bar{\nu}$ 1650 falls in a region very close to the water band excited by the 4047 A.U. mercury line. This adds to the confusion as to the real existence of this frequency shift—Silveira and Bauer notwithstanding. However, it may be again mentioned that one of the fundamentals to be expected from the water molecule according to Johnston and Walker (169) is $\Delta\bar{\nu}$ 1648, which does actually appear in the vapor state, but which apparently is completely absent in pure liquid water. Silveira (254) originally noted this shift in magnesium chloride and magnesium nitrate solutions but not in solutions of magnesium chlorate. It was first attributed to a probable hydrate formed by the magnesium ion.

Sterling and Laird (257) examined solutions of sodium nitrate at different concentrations, particularly with reference to the behavior of $\Delta\bar{\nu}$ 1049. No changes in this frequency shift were observed. It was presumed in highly concentrated solutions of sodium nitrate that the sodium nitrate molecules would exist in sufficient concentration to give a somewhat different spectrum than would be obtained from the nitrate ions alone.

Solutions of bismuth nitrate in nitric acid are highly complex, according to Ollano (211). This salt is hydrolyzed even in the presence of nitric acid. In addition to $\Delta\bar{\nu}$ 1414, 1032, and 720, $\Delta\bar{\nu}$ 980 was observed and attributed to the fourth fundamental frequency of the nitrate ion. $\Delta\bar{\nu}$ 1236 is doubtful. In addition to this, $\Delta\bar{\nu}$ 1600 and $\Delta\bar{\nu}$ 1500 observed were attributed to hydrolyzed bismuth, as previously discussed in the Raman effect of bases. The nitrates of lanthanum, cerium, and thorium have also been investigated (164).

TABLE 11

Inorganic solutions (carbonates)

SUBSTANCE	CONCENTRATION	RAMAN SHIFTS	REFERENCES
Na_2CO_3..................	1 *N*	1065	(117, 166)
K_2CO_3....................	1 *N*	1067 (1075)	(117, 129, 196, 166, 244)
$KHCO_3$..................	26 per cent	1035	(196)

Carbonates

Embirikos (117) observed that in 1 *N* and 2 *N* aqueous solutions the frequency shift of the alkali carbonates corresponding to the inactive vibration is slightly less in solution than in crystals.

The configuration of the carbonate ion approximates that of the nitrate ion. Only the shift corresponding to the symmetrical oscillation has been recorded so far. These are given in table 11. This shift is appreciably lower in the acid carbonate than in the carbonate. The lines characteristic of carbon dioxide gas have no counterpart in these solutions. As is to be expected, there is no shift corresponding to the $C \leftrightarrow H$ vibration.

The sulfites will be discussed under the sulfur compounds, table 14.

C. TYPE XO_4

The Raman shifts given in table 12 for a variety of compounds of the general type XO_4 are admittedly incomplete. Nor are the

TABLE 12

Inorganic solutions (type XO_4*)*

SUBSTANCE	CONCENTRATION	RAMAN SHIFTS*	REFERENCES
NaH_2PO_4	38 per cent	358 518_m 889_s 1061_m	(208)
Na_3VO_4	14	875 (907)	(208, 199)
Na_2CrO_4	13	855_m	(208)
Na_2WO_4		371_w (583) 931_w 1017 1394 1540_w	(208, 199, 233)
Na_2MoO_4	17	330_m (314) 845_m 898_s	(208, 233)
Na_2SeO_4	17	335 432 830_s	(208)
Na_3AsO_4	7	349 462_w 837	(208, 199)
K_2WO_4	26	933_s	(208)
$(NH_4)_2MoO_4$		256 356 885_w 938_s	(208, 199)
H_2TeO_6	15	648_m	(208)

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* See footnote to table 8.

estimates of relative intensities very accurate. The individual differences in similar compounds which may exist in two forms, such as, for example, sodium arsenite and sodium arsenate, are strikingly marked. The progressive change from the metavanadate to orthovanadate structure has already been mentioned. In addition, Ghosh and Das (199) point out that the neutralization of an alkaline solution of the sodium tungstate causes a marked decrease in the intensity of the Raman spectrum obtained from this compound. No lines were observed for silicic or molybdic acids. Nisi (208) observed that the principal Raman frequency shifts for compounds of the type Na_2SO_4, Na_2SeO_4, and H_6TeO_6 decrease with increasing atomic number. The respective principal shifts for these three compounds are $\Delta\bar{\nu}$ 979, 830, and 648. On the contrary, however, compounds of the type Na_2CrO_4, Na_2MoO_4, and Na_2WO_4 show increasing wave-number shifts with increasing atomic number, the respective principal $\Delta\bar{\nu}$ being 855, 898, and 931. Nisi ascribed this contradiction to a different distribution of extranuclear electrons, the mode of binding of the central atoms to the surrounding oxygen atoms being different for the two groups.

The solution of NaH_2PO_4 gives one strong line which nearly coincides with that due to the H_2PO_4 group, obtained from the ionization of H_3PO_4. No lines could be observed in a solution of Na_3PO_4.

Sulfates

The average fundamental frequency shifts for the sulfate ion observed by Ramaswamy (251) are $\Delta\bar{\nu}$ 457, 617, 981 and 1102, of which the first and third are inactive and the other two are active frequencies. The solutions studied comprise the sulfates of sodium, potassium, ammonium, magnesium, zinc, cadmium, and aluminum. Within the limits of the accuracy of measuring these frequency shifts, no definite changes were observed with different cations, in contrast to the observations with crystalline sulfates. On the whole, the magnitudes of the displacement are slightly less than those observed with crystals. Krishnamurti (133) observed that a saturated solution of ferrous sulfate gives the $\Delta\bar{\nu}$ 980 shift in the usual position, in contradistinction to his observation for the crystalline ferrous sulfate, where it was weak or entirely absent. As has been pointed out previously, the observation with respect to the crystals is open to doubt. The average frequency shifts for the SO_4 ion, as indicated above, have been confirmed by Fadda (198).

Embirikos (117) investigated the effect of concentration on the shift approximately represented by $\Delta\bar{\nu}$ 980. There is certainly a diminution in the magnitude of the shift in going from crystal to solution. Crystalline lithium sulfate, for example, gives $\Delta\bar{\nu}$ 1003, a 1 *N* solution of the same compound, $\Delta\bar{\nu}$ 989, and a 2 *N* solution, $\Delta\bar{\nu}$ 999. As the crystalline compound, however, becomes more hydrated, the magnitude of the frequency displacement becomes less, and more nearly comparable with that of a fairly dilute solution. The crystalline compound, $MgSO_4 \cdot 7H_2O$, gives $\Delta\bar{\nu}$ 987. A 1 *N* solution of $MgSO_4$ yields $\Delta\bar{\nu}$ 986, and a 2 *N* solution, $\Delta\bar{\nu}$ 996. The average value for the dilute solutions of all the compounds studied is slightly greater than those observed by Ramaswamy (251). This seems to be without significance, and may be due to a systematic difference in measurement. While there is a noticeable increase in the magnitude of this displacement with increasing concentration, the amount of this increase is reasonably uniform, being approximately ten wave numbers. Under ordinary conditions of measurement the reproducibility is usually not less than five wave numbers. The higher frequency shifts appearing in ammonium sulfate are attributable to the ammonium group rather than the sulfate group (208, 255). Nisi (146) observed no essential difference in the magnitude of the frequency shifts for manganous sulfate at different concentrations, but did observe a slight increase in $\Delta\bar{\nu}$ 980 for the aqueous solution of ferrous sulfate as compared with the crystalline compound, $FeSO_4 \cdot 7H_2O$. The results found with nickel sulfate would indicate a slight decrease, amounting to approximately five wave numbers for the solution as compared with the crystalline $NiSO_4 \cdot 7H_2O$.

It must be reiterated that these slight differences, except in cases where such observations are the main subject of experiment, are not to be given too much weight.

TABLE

Inorganic solutions (sulfates)

SUBSTANCE	CONCENTRATION	RAMAN SHIFTS*										REFERENCES
Li_2SO_4	18 per cent		442	593		984_s	1110_m					(208, 117, 218)
Na_2SO_4	Saturated		460_m	615		981_s	1101					(251, 117, 198, 208, 247, 219)
K_2SO_4	Saturated		457_m	619		981_s	1090					(251, 208)
$(NH_4)_2SO_4$			454_m	618		982_s	1107	1285_w		1467		(117, 251, 184, 208, 255, 212, 196)
$K_2Al_2(SO_4)_4$			477	607	(790)	977_m	(1160)					(241, 125, 146, 127)
$CuSO_4$		279?	429	610_m	717 – 754	980_s	(1058	1110	1143)	1472	1665	(247, 241, 184, 146, 127, 244, 233)
$MgSO_4$			456_m	617	(706)	982_s	1116					(247, 208, 218, 251, 117, 127)
$BeSO_4$			442_m	613		980_s						(146)
$ZnSO_4$			454_m	620		982_s	1106					(208, 251, 117)
$CdSO_4$			451_m	621		983_s	1108					(208, 251, 117)
$Al_2(SO_4)_3$			457_m	614		980_s	1104					(247, 251)
$MnSO_4$	1 *N*		452_m	613		988_s						(117, 218, 146)
$FeSO_4$	3 *M*, Saturated	(381)		673		978_m						(133, 95)
$NiSO_4$						980_s						(146)

* See footnote to table 8.

Silveira (184) observed several new lines in the Raman spectrum of copper sulfate, which is apparently more complex than the other sulfates. $\Delta\bar{\nu}$ 1110 apparently has two other adjacent frequencies, the three composing a triplet. The shifts corresponding to $\Delta\bar{\nu}$ 1472 and 1665 are probably not attributable to the copper sulfate. The doublet $\Delta\bar{\nu}$ 717 and 754 has been recorded as a single line by Hollaender and Williams (127) at $\Delta\bar{\nu}$ 723. The tendency to the splitting of frequencies in copper sulfate into doublets and triplets is particularly noticeable in the crystal (146), but was not observed by him in solutions of copper sulfate.

Sulfur compounds

The constitution of some of the complex compounds of sulfur in solution may be at least partially determined by using the same method of approach as that employed with the acids. The data upon which such an analysis may be predicated are given in table 14. On first inspection, it is apparent that there are certain similarities in the spectra of these substances, but it is also equally evident that there are many dissimilarities, and a detailed analysis is necessary to correlate the results.

To begin with, however, it may be pertinent, in order to make the picture more complete, to record the characteristic shifts of liquid SO_2, SO_3, and S_2O_6. For SO_2, the average values, $\Delta\bar{\nu}$ 525, 1145, and 1340 are obtained (197, 209, 226, 227, 232). Of these three shifts the central one is by far the strongest. For SO_3, $\Delta\bar{\nu}$ 535, 1068, and 1403 are observed (12, 226, 227). To S_2O_6, Bhagavantam (226, 227) attributes $\Delta\bar{\nu}$ 290, 370, 666, 697, 1271, and 1489. It is not to be expected that the SO_3 ion will give a spectrum identical with that of SO_3 liquid or SO_3 gas. There is naturally a greater dissimilarity between the uncharged gas and the SO_3 ion than there is between such an ion in the crystal lattice and such an ion in solution.

The early attempts to determine the Raman spectra characteristic of the sulfite ion led only to the distinguishing of the relatively strong line (208) at $\Delta\bar{\nu}$ 968. This is appreciably lower than that observed by Dickinson and Dillon (196) at $\Delta\bar{\nu}$ 988. Fadda (198) assigned $\Delta\bar{\nu}$ 471, 602, and 984, all of which fall remarkably close to the frequencies observed for the sulfates with the exception of the shift $\Delta\bar{\nu}$ 1110, which was absent.

As has been discussed under the Raman spectra of acids, an aqueous solution of sulfur dioxide gives the spectrum of sulfur dioxide rather than sulfurous acid. The sodium sulfite solutions, however, show no similarity to this behavior.

The existence of the ion HSO_3 is subject to some dispute. Ghosh and Das (199) assign the frequencies $\Delta\bar{\nu}$ 346, 826, 963, and 1406 to this ion in a solution of $NaHSO_3$. As has been previously mentioned, this ion is probably not present in sulfurous acid, although Nisi (209) tentatively assigned $\Delta\bar{\nu}$ 1054 to the HSO_3 ion and 1017 to the SO_3 ion, observed in the sulfurous acid solutions. The latter, together with the tentative assignment of $\Delta\bar{\nu}$ 1199 by Fadda to HSO_3, are probably erroneous.

Foerster, Brosche, and Norberg-Schulz (237) have determined the non-existence of the acid sulfites of sodium and potassium in the solid state, although there is a crystalline double salt corresponding to $K_2S_2O_5 \cdot 4KHSO_3$.

Before considering HSO_3 ions further, it may be pointed out that they can be formed (237, 245) according to the equation,

$$S_2O_5^{-} + H_2O \rightleftarrows 2HSO_3^{-}$$

and hence are somewhat intimately connected with the Raman spectrum of S_2O_5 ions.

It is the contention of Fadda (236) that $NaHSO_3$ does not exist in solution, the Raman spectrum of this compound indicating only the presence of S_2O_5 ions. Nisi (208) determined the Raman spectrum of a 17 per cent solution of $Na_2S_2O_5$ and obtained $\Delta\bar{\nu}$ 236 (s), 426 (m), 571 (w), 652 (m), 1015 (w), and 1054 (s), where s stands for strong, m for medium, and w for weak. Fadda obtained for a solution of supposed $NaHSO_3$, prepared according to the method of Muspratt (248, 249), $\Delta\bar{\nu}$ 242 (vs), 420 (m), 656 (s), and 1009 (vs). It is to be noted that $\Delta\bar{\nu}$ (427), 593, (978), and 1048 are present in the spectrum of $KHSO_4$ (208, 225). It is the contention of Fadda, therefore, that the $\Delta\bar{\nu}$ 571 and 1054 shifts observed by Nisi in $Na_2S_2O_5$ in reality owe their origin to the presence of HSO_4^-. To prove

TABLE 14

Inorganic solutions (sulfur compounds)

SUBSTANCE	CONCENTRATION	RAMAN SHIFTS*														REFERENCES
$KHSO_4$	12 per cent 28 per cent			427		593				978_m		1048_s				(208, 225)
$NaHSO_3$?		(314)	346						826	963				1406		(236, 199)
Na_2SO_3	16 per cent									968_m						(208)
Na_2SO_3	Saturated			471			602			984_m						(198)
K_2SO_3	52 per cent									988_m						(196)
K_2SO_3	20 per cent									968_m						(208)
$Na_2S_2O_3$			335	448_s		543	665			998_s		(1078)	1129_m			(212, 146, 208)
$Na_2S_2O_4$	17 per cent			407	458					983_m		1057_m				(208)
$Na_2S_2O_5$	17 per cent	236_s		426_m		(571)	652_m				1015	$(1054)_s$				(208, 236)
$Na_2S_2O_6$	Saturated	279						709_m				1090_s				(212)
$K_2S_2O_7$	12 per cent					585				980		1052_m				(208)
$(NH_4)_2S_2O_8$	25 per cent	216	322			557			836	971	1027	1076	1290			(208)
$Na_2S_2O_8$									833_m			1081_m				(199)
NaHS															2575_s	(199)

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* See footnote to table 8.

this point the experiments were carried out without contact with air. The solution showed no test for sulfate before or after experiment. No traces of $\Delta\bar{\nu}$ 571 or 1054 were observable. This leaves then a reasonably good agreement between the Raman spectra of $Na_2S_2O_5$ (as determined by Nisi with these corrections) and supposed $NaHSO_3$, the logical conclusion being the non-existence of $NaHSO_3$ in solution. There is, however, one factor which should be mentioned, namely, if $\Delta\bar{\nu}$ 1054 observed in the spectrum of $Na_2S_2O_5$ is to be attributed to air oxidation, then the inevitable conclusion is that Nisi's solution must have been largely oxidized, since this was the strongest line observed by him. In addition to the frequencies given, for the S_2O_5 ion, Fadda observed $\Delta\bar{\nu}$ 314 in a 50 per cent solution, but this was absent in a 17 per cent solution. This was attributed to a polymer of $Na_2S_2O_5$. In addition, $\Delta\bar{\nu}$ 1142, characteristic of sulfur dioxide, was also present. These results are not compatible with those of Ghosh and Das (199).

The next more complicated compound in the series is $Na_2S_2O_3$. The similarity between the spectrum of this compound and that of the sulfates is marked. This is most reasonably explicable on the assumption that the S_2O_3 ion has a constitution similar to the sulfates, that is, with one oxygen replaced by a sulfur atom and the other oxygen atoms being bound to one sulfur atom only. These results may be compared with the shifts observed by Nisi (146) for crystalline $Na_2S_2O_3 \cdot 5H_2O$. These were $\Delta\bar{\nu}$ 324, 433 (s), 546, 612, 674, 1018, 1116, and 1162. With allowance for possible lattice frequencies and the tendency to split frequencies in crystals, the results, as compared with those obtained from solutions, are reasonably compatible. Each of the lines corresponding to the two active vibrations clearly splits into more than one component. The relative intensities, however, of the inactive vibrations for S_2O_3 are the reverse of those which exist in the case of the sulfates.

According to Pringsheim and Yost (212) for the S_2O_6 ion the oxygen atoms are symmetrically arranged in respect to each sulfur atom, giving the formula $O_3S—SO_3$. It may be mentioned that the characteristic frequency of the $S \leftrightarrow S$ vibration in the organic disulfides, such as methyl disulfide, occurs (260) at $\Delta\bar{\nu}$ 512, for which there is no counterpart in the S_2O_6 ion.

The compound $Na_2S_2O_4$ can be equally well written $NaSO_2$. In the presence of water only slightly above room temperatures it may be converted into $Na_2S_2O_3$ and $NaHSO_3$. The Raman spectrum is not consistent with the formula $NaSO_2$ since the dissociation of this compound would lead to a spectrum more similar to that of SO_2 than the one observed. From an analogy of the similarity of the spectrum with that of the sulfates, it might be presumed that the oxygens are attached to one rather than both sulfur atoms.

The compound $K_2S_2O_7$ in solution gives, according to Nisi (208), a Raman spectrum which nearly coincides with that given by $KHSO_4$. This is not surprising when one considers that $K_2S_2O_7$ is obtained by dehydrating two molecules of $KHSO_4$, and probably results, on solution, in the formation of HSO_4 ions.

Compounds of the type giving S_2O_3 ions have been insufficiently studied as yet from the point of view of Raman spectra to provide more than a basis for pure speculation.

Nisi (209) has attempted to determine the characteristic frequency vibrations of the SO_2 and SO groups from the spectrum of the organic sulfonic acids, chlorosulfonic acid, sulfuryl chloride, sulfur oxychloride, and organic sulfites. He concluded that at least one line between $\Delta\bar{\nu}$ 1130 and 1190 was characteristic of the SO_2 group in the combination and that possibly $\Delta\bar{\nu}$ 1220 was characteristic of the SO group.

It is difficult to correlate these conclusions with the other data. The organic derivatives, such as benzenesulfonic acid, have sufficiently complicated spectra themselves, and the assignment of a specific frequency to a specific group is increasingly difficult. Since the molecular species in acids will vary with dilution, it is also precarious to use these substances as standards.

In summarizing, it may be stated that these Raman spectra studies, while as yet in most cases incomplete, provide a fair amount of information concerning the constitution of complex sulfur compounds in solution. Salts of the type $R-SO_3$, unlike the acids, have a definite constitution and configuration. The existence of an acid sulfite in solution is an open question. It is possible that the compound exists as $S_2O_5^=$ rather than HSO_3^-. On the contrary, salts of the type $K_2S_2O_7$ in solution may exist as HSO_4 ions. Certainly the binding force between the sulfur and the oxygen atoms in all of the compounds is of the same order, and the ionization of the HSO_4 ion to SO_4 is likewise indicated. To compounds giving ions of the type S_2O_3, S_2O_4, and S_2O_6, from symmetry considerations and their similarities and dissimilarities to sulfates, can be ascribed a fairly reasonable constitution.

These compounds have not been investigated and reinvestigated by different observers. In time a clearer and more accurate picture will undoubtedly be obtainable. It must not be forgotten that partially, at least, such interpretations are predicated on analogies and extrapolations. Often these may be accepted as factual and can be considered reasonably accurate. In the case of the sulfur compounds, however, accurate fundamental information concerning them from the point of view of inorganic chemistry is meagre. In any case, whatever interpretation may be ultimately accepted, the data obtained from the point of view of Raman spectra must be quantitatively accounted for.

Perchlorates

Since the mass of the chlorine and the configuration of the chlorate ion are approximately identical with those of the sulfate ion, the Raman shifts should closely approximate those obtained for the sulfates provided the binding force between the oxygen and sulfur is nearly the same as that between chlorine and sulfur. It can be seen from table 15 that this is the case. The strongest shift, averaging $\Delta\bar{\nu}$ 934, is approximately fifty wave numbers less than the equivalent displacement observed with the sulfates. Ollano (210) observed two large frequency shifts at $\Delta\bar{\nu}$ 3544 and 3599. The former he attributed to H_3O^+ and the latter to $H(H_2O)_n^+$.

For KIO_4 $\Delta\bar{\nu}$ 702 probably represents the inactive frequency and is shifted considerably lower, owing to the increased mass of the iodine atom.

TABLE 15

Inorganic solutions (perchlorates)

SUBSTANCE	CONCENTRATION	RAMAN SHIFTS*	REFERENCES
	moles per liter		
$NaClO_4$	10.8	463_w 626_w 935_s 1120_w	(177, 210)
$KClO_4$	0.14	461 632 936_s	(177, 210)
NH_4ClO_4	1.9	463 626 930_s 1109	(177, 210)
KIO_4		702_m	(208)

* See footnote to table 8.

Halogens

In table 16 are given the Raman frequency shifts observed for polyatomic halogen derivatives. Those halogen derivatives which occur as liquids will be considered separately. Those compounds which ionize completely in solution give no Raman lines which may be attributed to an anion-to-cation oscillation. The large frequency shifts from $\Delta\bar{\nu}$ 1600 upwards (if real) are presumably due to perturbations between the ions and water, as previously discussed. Cadmium chloride shows evidence of homopolar binding in solutions, as do the chlorides of zinc, mercury, magnesium and bismuth. The $\Delta\bar{\nu}$ given for ammonium chloride may be associated with the NH_4 group. A progressive decrease in the magnitudes of the shifts for the chlorine, bromine, and iodine derivatives of mercury is attributable to the increased mass of the respective anions.

A concentrated solution of mercuric chloride in methyl alcohol gives a shift at approximately $\Delta\bar{\nu}$ 275 according to Krishnamurti (132), or in practically the same position as that observed in the crystals but considerably broadened. Crystalline zinc chloride was also observed to give a faint line at $\Delta\bar{\nu}$ 234. Unlike mercuric chloride, which was considered to be a linear model by Krishnamurti, zinc chloride was presumed to be triangular.

Aqueous solutions of zinc chloride were investigated by Hibben (125) over a hundredfold concentration range. With concentrated solutions $\Delta\bar{\nu}$ 297 and 396 were observed, the former shift having an intensity approximately six times greater than the latter. Between concentrations of 11 molal and 1 molal these

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K_2HgCl_4								229		
K_2HgBr_4								229		
K_2CdBr_4	--							230		
K_2HgI_4.	26							229		
$KCdI_3$..	18,							229		
Na_2CdI_4	09							230		
$MgCl_2$..			376		785			254,	256	
NH_4Cl..								255		
$HgCl_2$..			320					136,	228,	22
$HgBr_2$..		205						228,	230	
HgI_2...								229,	230	
$BiCl_3$....		242	289,					235,	23,	
Al_2Cl_6..			348	54				(125		
$ZnCl_2$...		297_w	396_s					125		
$LiCl$....						658	762	256		
$CdCl_2$..	3	243						256,		
CdI_2.....								(230		
$CaCl_2$...						65		256		
$SrCl_2$....										

ootnote

relative intensities remain approximately the same, although there is a sharpening of both lines with dilution. With further dilution, however, the ratio of the intensity of $\Delta\bar{\nu}$ 297 to that of $\Delta\bar{\nu}$ 396 becomes much less, the two lines having approximately equal intensity at a concentration of half molal. There may also be other lines present in the very dilute solutions. If the stronger line is attributed to the linear oscillation of a chlorine atom against a ZnCl group and the weaker one is attributable to a chlorine atom oscillating against a zinc atom in a ZnCl ion, then this behavior is reasonably explicable since the more concentrated solution consists largely of undissociated zinc chloride and the more dilute solution has a higher concentration of the ZnCl ion. This is in agreement with the stepwise dissociation of zinc chloride as determined by conductivity measurements (242, 250, 252).

Aqueous solutions of Al_2Cl_6 give $\Delta\bar{\nu}$ 348, 541, and 808, the middle shift being the strongest, according to Hibben (125). The latter two of these are identical with the shifts obtained from anhydrous Al_2Cl_6 crystals, $\Delta\bar{\nu}$ 348 being indeterminable in the crystalline material. It is presumed from this that Al_2Cl_6 exists in aqueous solution in the polymerized form. From the point of view of inorganic chemistry its structure is open to question (246). Sidgwick considers (253) that the $AlCl_3$ molecules are coupled through two chlorine atoms by coördination. The relative simplicity of the spectrum would argue in favor of a symmetrical arrangement. Hydrated Al_2Cl_6 shows no Raman lines comparable with the anhydrous material, which is reasonable if one views the aluminum atom in this case as surrounded by water molecules, as has been shown to be the structure of some of the chlorides (262).

SUMMARY

The Raman spectra of solutions give frequency shifts corresponding to both solute and solvent. The frequency displacements of the solute are essentially those observed for crystals. When, however, the solute ionizes, only those Raman shifts are present which correspond to the polyatomic ion. If ionization takes place in successive stages, this is indicated. The so-called lattice vibrations observed in crystals are missing in solutions. The cation, however, is not without some influence in solution, but it is much less than that observed in crystals. The influence of the cation is further indicated by the occasional marked change in the Raman spectrum in passing from the salt to the acid form. The spectra observed from compounds containing the same anion but different cations are sometimes appreciably different. The change from the alkalies to the alkaline earths, for example, produces a much more complicated spectrum.

The frequency shifts corresponding to the symmetrical vibrations in an ion are appreciably less in solution than in the crystals. This would indicate a slight diminution of the force exerted between the atoms. The spacial configurations of the ions are somewhat analogous in gases of the same general type. Changes in valency produce marked changes in the Raman spectra of the respective compounds. The relative intensities of the lines vary with changing concentrations. The inactive shift for sulfate solutions more nearly approaches that of the crystal with increased concentration. Indeed, the displacement in a concentrated solution may exceed that of the corresponding crystal if the latter is highly hydrated. The similarity in spacial arrangement and in binding force between similar ions is marked. The polymerized form of certain crystals is sometimes retained in solution. The more complex sulfur compounds sometimes may retain the same form in solution as they possess in crystals or they may not do so, depending on the particular compound. If the material to be examined is sufficiently soluble, the Raman spectra of solutions offer a method of determining the constitution under conditions which often cannot be approached by any other means. Intermediate compounds and complex-compound formations in solution will be discussed in the succeeding section.

VIII. Raman Spectra of Complex-compound Formations

Complex compounds may exist in the vapor, liquid, or solid states of aggregation or in solution. By complex compound is meant those molecules, alike or unlike, which may combine to form double polymers, mixtures, coördinated complexes, and quasi compounds, whose real existence has been more or less hypothetical. The Raman spectra method in many cases is a unique means of determining the existence of certain types of complexes. In true mixtures the Raman spectrum of each compound is approximately independent of others. If, however, there is an actual interaction, the normal Raman spectra will be considerably affected. A more or less classical example of this is in polymerization. This is evidenced, for example, in the polymerization of sulfur trioxide. Chemical evidence shows the presence of two varieties of sulfur trioxide, having a distinct melting point, one consisting of the polymerized molecules with the formula S_2O_6, at low temperatures, and depolymerizing to SO_3 near 100°C. The Raman spectrum at room temperature consists of nine frequencies, according to Bhagavantam (226), which were attributed to the S_2O_6 molecule. On heating to approximately 100°C., six of these, namely, $\Delta\bar{\nu}$ 290, 370, 666, 697, 1271, and 1489, become considerably weaker, and the remaining three, $\Delta\bar{\nu}$ 535, 1068, and 1489, become distinctly stronger. The latter three frequencies are attributed to SO_3. This process is perfectly reversible, and may be repeated with identical results. Thus, polymerization of SO_3 and the depolymerization of S_2O_6 can be followed by means of the Raman spectrum of the components of this mixture.

In the solid state the Raman spectrum from the solid eutectic of $NaNO_3 + KNO_3$ shows only one sharp principal frequency for the NO_3 group when freshly prepared, according to Gerlach (264). After a period of approximately one day, however, the initially sharp line becomes gradually broad and diffuse, finally separating with increasing time into two sharp distinct lines, one having a frequency shift corresponding to that of sodium nitrate and the other to potassium nitrate. The initial sharp line obtained from the eutectic lies half-way between the two final lines attributed to sodium nitrate and potassium nitrate, respectively. X-ray diffraction patterns showed no difference between samples at different ages, and the results are independent of the rate of cooling. It might be mentioned, however, that

KNO_3 I first changes metastably to KNO_3 III, which then inverts to KNO_3 II, according to Kracek (266, 267). Whether or not this has any connection with the suppositions of Gerlach is a matter for further investigation.

Proof of the formation of mixed molecules by the use of the Raman effect has been demonstrated by Trumpy (270, 271). The procedure was first to determine the Raman shifts for pure compounds, such as phosphorus trichloride and phosphorus tribromide. These were then mixed with varying ratios and the Raman spectra of the mixtures determined. These mixtures give rise to new Raman lines which change in intensity with the amount of each compound. With ratios of two parts phosphorus trichloride and one part phosphorus tribromide, and one part phosphorus trichloride and two parts phosphorus tribromide, the results showed two types of mixed molecules to be present, namely, PCl_2Br and $PClBr_2$. The $\Delta\bar{\nu}$ found for phosphorus trichloride are $\Delta\bar{\nu}$ 190, 256, 485, 510, and for phosphorus tribromide, $\Delta\bar{\nu}$ 115, 161, 379, and 397, of which the lowest shifts are the strongest. Mixtures of silicon tetrabromide and stannic bromide showed no new lines. The system $SnCl_4$–PBr_3 shows the presence of $SnBr_4$, PCl_3, $PClBr_2$, PCl_2Br, $SnCl_3Br$, $SnCl_2Br_2$, $SnClBr_3$. These results are given graphically in figure 16.

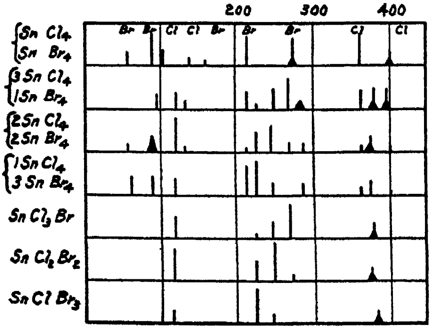

FIG. 16. RAMAN SPECTRA OF MIXED MOLECULES
(After Trumpy)

Krishnamurti (136) observed $\Delta\bar{\nu}$ 313 (s) and $\Delta\bar{\nu}$ 381 (w) for mercuric chloride crystals. In solution, with one mole mercuric chloride and one mole ammonium chloride, were observed $\Delta\bar{\nu}$ 274 and $\Delta\bar{\nu}$ 313, both lines being broad and diffuse with the former stronger than the latter. With one mole mercuric chloride and two moles ammonium chloride only $\Delta\bar{\nu}$ 269 was observed. With crystalline $(NH_4)_2HgCl_4$ $\Delta\bar{\nu}$ 273 was obtained. With a mixture, therefore, of the composition $HgCl_2$, $2NH_4Cl$, whether in solid state or in solution, a Raman line $\Delta\bar{\nu}$ 269 is observed, characteristic of the complex salt $(NH_4)_2HgCl_4$. Any mercuric chloride in excess of this composition gives its own line characteristic of mercuric chloride, namely, $\Delta\bar{\nu}$ 313, thus demonstrating the existence of this complex in solution. These results are quite similar to those obtained by Braune and Engelbrecht (228, 229) with solutions of mercuric halides and potassium chloride.

There is some evidence for the existence of solid inorganic polymers. Krishnamurti (130) attributes the existence of a faint Raman line, which appears in crystals of lithium, mercuric, and aluminum nitrates, and which is shifted between ten and twenty wave numbers from the strong inactive frequency, to the effect of polymerization of the molecule in a solid state. These faint components appear at $\Delta\bar{\nu}$ 1052 for lithium nitrate, $\Delta\bar{\nu}$ 1021 for mercuric nitrate, and $\Delta\bar{\nu}$ 1058 for aluminum nitrate. In the first two cases this appears on the shorter wave length side of the principal line, while with aluminum it appears on the opposite side. In the case of aluminum nitrate, the strong line is attributed to the polymerized molecule and the fainter line to the simple one. With lithium nitrate and mercuric nitrate the strong shift is attributed to the monomeric form and the weak to the dimeric. This component does not occur in concentrated solutions of lithium nitrate. In view of the subsequently observed splitting of Raman shifts in other compounds, due to degeneracy, it is not altogether certain that the explanation given by Krishnamurti would now be considered by him as the most probable one. The polymerization of aluminum chloride and esters of silicic acid has already been discussed (125, 159, 160).

The existence of complex compounds in solution is a particularly interesting phase of Raman spectra investigation, which may be illustrated in the following examples. A solution of mercuric chloride in methyl alcohol gives $\Delta\bar{\nu}$ 319, which is considerably broadened in comparison with the shift $\Delta\bar{\nu}$ 313, observed in mercuric chloride crystals, but no obvious change was noted in the spectrum of methyl alcohol by Krishnamurti (136). Solutions of zinc chloride in methyl alcohol were observed by Hibben (125) to result in a modification of the methyl alcohol spectrum and apparently in a suppression of the normal zinc chloride lines. The time of exposure which normally brings out the characteristic shifts of zinc chloride in an aqueous solution or in ethyl alcohol solution, failed to elicit any lines for zinc chloride, in a methyl alcohol solution containing one mole of zinc chloride to two moles of methyl alcohol. So far as the alcohol is concerned, however, $\Delta\bar{\nu}$ 1036, characteristic of the C↔OH was shifted to a lower value by twenty-two wave numbers, and $\Delta\bar{\nu}$ 2841 and 2945 were shifted to a higher value by twenty-three wave numbers. The most pronounced effect was the diminution in intensity of $\Delta\bar{\nu}$ 1472, characteristic of the transverse oscillation of C↔H. If the oscillation frequency of the zinc chloride were shifted considerably to a much lower frequency, the Raman line would not be observable on account of the general scattering of the exciting radiation. On the other hand, the effect of the interaction between zinc chloride and methyl alcohol may be to make less probable the normal transitions which give rise to the normal frequency shifts in zinc chloride. A somewhat similar and more pronounced effect was noted in alcoholic solutions of Al_2Cl_6. In contrast to this behavior, solutions of zinc chloride in ethyl alcohol gave $\Delta\bar{\nu}$ 300 (s) and $\Delta\bar{\nu}$ 308 (w). The former shift is approximately that observed for zinc chloride in aqueous solution. However, $\Delta\bar{\nu}$ 308 was not observed in aqueous solution, and $\Delta\bar{\nu}$ 396, observed in aqueous solution, was missing. It may be reiterated that $\Delta\bar{\nu}$ 300 was attributed to un-ionized zinc chloride, and $\Delta\bar{\nu}$ 396 was attributed to the oscillation of the remaining ion after partial ionization of the molecule. As the degree of ionization is small in ethyl alcohol solutions, this difference between aqueous and ethyl alcohol solutions is understandable. The observed difference between crystalline zinc chloride (131), which gave $\Delta\bar{\nu}$ 234, and the shift observed from solutions is quite marked and beyond experimental error. These experiments point to complex-compound formations in solution. It might be added that x-ray investigations of alcoholic solutions of alkali halides indicate some type of compound formation (269).

The spectrum obtainable from complex copper compounds has been investigated by Bose and Datta (263). The compounds $[Cu(NH_3)_5Cl]Cl_3$ and $[Cu(NH_3)_6]Cl_3$ give a modified line at approximately $\Delta\bar{\nu}$ 568. The compound $[Cu(NH_3)_6]Cl_2$ gave no modified line. The interest was primarily in the vibrations of the complex. The compound $[Cu(NH_3)_6]Cl_3$ was considered a true coördination compound. The spectrum is doubtless incomplete.

Copper, zinc, and cadmium ammonium complexes have been investigated by Joos and Damaschun (265) and Damaschun (233). It is argued that there exists a certain similarity between hydrated salts and ammino compounds. To verify this, comparison was made between aquo compounds and the ammino compounds by the analysis of characteristic oscillations. In none of the salts investigated, however, in aqueous solutions in which the existence of a definite hydrate is assumed, could a Raman line be detected corresponding to the aquo complex. An aqueous solution of copper sulfate gave $\Delta\bar{\nu}$ 434, 600, 979, and $\Delta\bar{\nu}$ 1096. With the corresponding ammino compounds, with two exceptions, an oscillation near $\Delta\bar{\nu}$ 400, characteristic of the complex, was observed. The results are given in table 17.

Ammonium compounds of silver and nickel gave no Raman lines characteristic of the complex. The $\Delta\bar{\nu}$ for the NH_3 group in the complex is appreciably lower than that obtained from pure NH_3. The frequency displacement for either the complex zinc chloride or complex zinc sulfate becomes less on standing over a period of time, the presumption being the conversion of the hexammino compound to the tetrammino compound under these circumstances.

Freshly made $Zn(NH_3)_6Cl_2$ gives $\Delta\bar{\nu}$ 418. A compound of the composition $(NH_4)_4(ZnCl_6)$ gives $\Delta\bar{\nu}$ 274, which was attributed by Damaschun to the anion $(ZnCl_6)^{\equiv}$. This can be written, however, as $ZnCl_2 \cdot 4NH_4Cl$, wherein $\Delta\bar{\nu}$ 274 may be attributed to the Raman spectra of zinc chloride. The frequency, however, is slightly less than that observed in zinc chloride solutions ($\Delta\bar{\nu}$ 296). Only the strong inactive frequency of the SO_4 group was recorded in the complex zinc and copper sulfates. These were for $Cu(NH_3)_4SO_4$, $\Delta\bar{\nu}$ 977, and for $Zn(NH_3)_6SO_4$, $\Delta\bar{\nu}$ 979 and 1110. No lines were observed which could be attributed to an interchlorine vibration. The absence of frequencies which could be attributed to aquo complexes does not necessarily entirely preclude their existence. They may be too broad to be detected, or, as a result of loose binding, only one excitation stage of oscillation may exist.

TABLE 17

Characteristic Raman frequencies of ammino compounds

COMPOUND	INNER VIBRATION OF COMPLEX	AMMONIA VIBRATIONS
	$\Delta\bar{\nu}$	$\Delta\bar{\nu}$
NH_3	—	3223 3306 3394
$Cu(NH_3)_4SO_4$	410	3309
$Cu(NH_3)_4Cl_2$	419	—
$Ni(NH_3)_6Cl_2$	—	3286 3374
$Zn(NH_3)_6Cl_2$	418	3183 3274
$Zn(NH_3)_6SO_4$	428	3193 3268
$Cd(NH_3)_6Cl_2$	340	3287 3372
$Ag(NH_3)_2Cl$	—	3305

Although the cyanides will be discussed briefly under a separate title, two complex cyanides were observed by Damaschun (233) to give shifts ostensibly characteristic of the complex. These are for $K_3Co(CN)_6$, $\Delta\bar{\nu}$ 340, for $K_3Cr(CN)_6$, $\Delta\bar{\nu}$ 728. However, complex iron, zinc, cadmium, and copper cyanides gave no such displacement. This is also true of $K_2Hg(CN)_4$ (229). The compounds $K_4Ru(CN)_6$, $K_3Rh(CN)_6$, (268) and for $KAg(CN)_2$, (229) have low frequency shifts.

As has been mentioned, compounds of the type K_2HgCl_4 give a well-defined Raman shift. On the other hand, compounds of the types $KCdCl_3$ and $KAgI_2$ give no Raman lines (229). This is presumably connected with the nature of the homopolar binding. The compound $KCdI_3$ gives an especially strong line at $\Delta\bar{\nu}$ 118, attributed to the complex. Complex molybdates and tungstates have been investigated by Damaschun (233) with the results indicated in table 18.

For the molybdates, the corresponding largest frequency shifts are sharp and intense. The intermediate shifts are broad and weak. The displacement of $\Delta\bar{\nu}$ 314, which occurs only in Na_2MoO_4, is broad and strong. Apparently with increasing complexity of the molecular aggregation there is a gradual increase in the magnitude of the larger shifts. Whether or not the aggregations have the formulas assigned to them is another question. The Raman spectra in any case show a measurable alteration.

TABLE 18

Some Raman frequencies of tungsten and molybdenum complexes

SUBSTANCE	$\Delta\bar{\nu}$
Na_2MoO_4	314 843 896
$Na_4Mo_3O_{11}$	— 886 937
$Na_6Mo_6O_{21}$	— 913 959
$Na_{10}Mo_{12}O_{41}$	— — 953
Na_2WO_4	583 930 —
$Na_6W_6O_{21}$	— 961 —

SUMMARY

The existence of complexes in the gaseous, liquid, and crystalline states of aggregation or in solution, including polymers, more or less definite compounds, and those compounds whose existence is too ephemeral to determine by chemical means, has long been postulated on the basis of the other physical and chemical data. The investigation of these complexes from the point of view of the Raman effect provides a new method of approach which, in time, doubtless will bear considerable fruit. As can be stated of many of the Raman studies, the results are as yet incomplete. Nevertheless, sufficient data have accumulated to aid in the interpretation of the constitution of these substances, particularly in those cases where other methods are inadequate. Nor does this interpretation rest solely on the Raman spectra of inorganic complexes. From the point of view of organic chemistry it may be demonstrated even more clearly that these interpretations are, in general, correct. Organic polymers, whose constitution is very well known, give Raman spectra perfectly in accord with that constitution, and organic complexes which exist only in solution, likewise, in general, give Raman spectra consistent with the interpretation based upon the behavior of these complexes from an organic point of view.

IX. Raman Spectra of Amorphous Compounds and Mixtures

Amorphous materials have been less investigated from the point of view of Raman spectra than any other class of substances. The reason for this lies in the difficulty of eliciting Raman lines from such materials. This is because of the extreme feebleness of the Raman shifts from these compounds. Exposures from days to weeks are often necessary to record the strongest Raman lines. Furthermore, the most common amorphous substance, glass, is so complex that the interpretation of the Raman spectra obtained is very difficult. With improved experimental technique, particularly in the direction of monochromatism, improved optical systems, and greater light intensities, and finally with a systematic investigation of the more simple glasses and simple silicate compounds as a preliminary, it can be predicted that more comprehensive and fundamental information concerning the constitution of amorphous substances will be made available.

It has been shown that Raman shifts from crystals, liquids, gases, and solutions are characteristic of the valence forces, the atomic masses, and the spacial configurations of the molecule. Since amorphous substances also possess these properties, there is no *a priori* reason why they should be an exception. The difficulty probably lies in the imperfect quantization of the vibrational energy, and may be somewhat analogous to the effect of increased pressure, which will be treated later. The lines obtained from amorphous substances are broad and diffuse and can only be quantitatively investigated by microphotometric means. It may be emphasized, however, that notwithstanding these deterrents, the Raman spectra method offers an almost unique method of investigation for these substances which give no x-ray pattern and which will not yield to the usual physico-chemical methods of approach. The Raman shifts for a number of glasses and amorphous silicon dioxide (fused silica) as compared with crystalline silicon dioxide (quartz) are given in table 19.

The large number of observed frequencies in quartz can only be accounted for by the assumption of a large number of external vibrations, indicating a complicated lattice. So far as fused silica is concerned, it was originally believed that no Raman effect could be observed (149). Later, however, Gross and Romanova (122) obtained a large number of lines agreeing qualitatively with those obtained with the crystalline material. Apparently the intensity relations are not identical, although these estimates are, at best, qualitative.

One of the most intense lines observed in quartz, $\Delta\bar{\nu}$ 125, is missing in all the glasses and in fused silica. This may possibly be due to its close proximity to the exciting line and it may consequently be hidden behind the general background scattering. This point possibly could be clarified by excitation with the 2536 A.U. mercury line and the reabsorption of this line with mercury vapor, at least so far as fused silica is concerned. Any comparison between Raman spectra of the glasses from an intensity point of view is particularly difficult in view of the well-known differences in absorption which small traces of impurity will impart to these substances. On the other hand, the magnitudes of the shifts show more than considerable similarity with that of the other compounds containing silicon dioxide, but at this time the absence of particular frequencies cannot be given great weight. It may be stated, however, that those glasses which have a high index of refraction show relatively greater intensities in the bands near $\Delta\bar{\nu}$ 1000 and $\Delta\bar{\nu}$ 1080 than the earlier members of the series. The same may also be said of the band lying between $\Delta\bar{\nu}$ 460 and 500. However, the relative intensity between these two groups ($\Delta\bar{\nu}$ 460–520 and $\Delta\bar{\nu}$ 1080 (max.)) suffers a reversal in passing

TABLE 19

Raman spectra of amorphous compounds

COMPOSITION	REFRACTIVE INDEXES	RAMAN SHIFTS*																									REFERENCES
Crystalline quartz......		125_s	207_m	264_w	(320)	358	405	463_s	503	526	585	633	694_w	(746)	800_w	943	1020	1075_w	1163	(1220)							(122)
Amorphous silica........			213	263	323	370		440_s	500			625_w	670	740	$800\text{-}830_m$			1030-1090		1190-1240							
Crown glass............			208	270	330	385		450-510				625	670	740	800-830			1030-1090	1140-1190								(272)
Fluor crown	1.4933							460																			
U. V. crown............	1.5035							480							780			1080									
Prism crown......	1.5163							460																			
Silicate crown..........	1 5191							$460\text{-}520_m$							800_w			1070_m			1320						
Flint glass.............			208	260	323	370	450		510		590		670	740	800	970		1050	1140	1190							(122)
Telescopic flint.........	1.5286							$460\text{-}520_s$							800			1080									(272)
Baryta light flint.......	1.5694							460				640_w			800			1065_m			1330						
Densest borosilicate crown...............	1.5726				340			460				650_w			800			1090_m			1320						
Ordinary light flint.....	1.5774							460-500							780_w		1000_s	1080_s			1320						
Baryta light flint.......	1 6042							$460\text{-}500_m$									1000_s	1080_s									
Ordinary flint..........	1.6202							$460\text{-}520_m$									1000_s	1080_s									
Plate glass.............				268											785			1070			1293		1657		1860	(2309)	(126)
75 per cent SiO_2																											
Plate glass.............				259				471	537			647			785			1071_s			1293	1585		1748			(127)
Pyrex glass.............							400								780												(180)

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* See footnote to table 8.

from the lower index glasses to the higher index glasses, although the absolute intensity of both groups is less in the lower index members. The increasing intensity of the Raman shifts with increasing index of refraction may possibly be attributable to the closer approach of the exciting radiation to the characteristic ultra-violet absorption in these glasses, that is, when the absorption frequency approaches the value $\frac{E_n - E_k}{h}$ where E_n is the energy of the "third level," discussed in the section on "Theory" (p. 351). Since the ultra-violet absorption is determined largely by the impurities present, this explanation may not be tenable. In some of the glasses larger frequency shifts between $\Delta\bar{\nu}$ 1293 and $\Delta\bar{\nu}$ 1748 appear which are not present in either amorphous or crystalline silica. These cannot be attributed to external vibrations. It is also extremely unlikely that these shifts would appear in the glasses and not in crystalline silica if their presence were possible in both materials. The shift $\Delta\bar{\nu}$ 2309, noted by Hollaender and Williams (126) is probably erroneous. $\Delta\bar{\nu}$ 1320, observed by Bhagavantam (272) appears in some of the glasses studied by him but not all. The absence is without significance.

It has already been mentioned that Weiler (159, 160) considers $\Delta\bar{\nu}_1$ 1170–1208, $\Delta\bar{\nu}_2$ 1062–1086, $\Delta\bar{\nu}_3$ 800, and $\Delta\bar{\nu}_4$ 502 as the fundamental vibrations of the SiO_4 group (276).

It has been shown by Bragg and Gibbs (273) and Wyckoff (278) that in quartz, for example, each silicate atom is surrounded by four oxygen atoms, giving nearly a tetrahedral structure, the group unit being, therefore, from the point of view of Raman spectra, SiO_4 rather than SiO_2. The problem, therefore, is really in relating the Raman spectra of amorphous silicates to other compounds containing an SiO_4 group, whose degree of polymerization can be more easily ascertained and whose composition can be more readily investigated by other physico-chemical processes.

The frequency shifts given above as characteristic of the SiO_4 group have been obtained from a systematic study of a series of esters of silicic acid. This investigation by Weiler (160) yielded the results given in table 20.

The structure and constitution of the esters has been investigated by Staudinger (277), Eulitz (274), and Konrad, Bächle, and Signer (275). The four frequencies given in the table were considered characteristic of the inner vibrations of the SiO_4 group. The changes in the frequency shifts were attributed to the influence of polymerization. In addition to a large change in magnitude, $\Delta\bar{\nu}_4$ also decreases markedly in intensity with increase in polymerization. The latter two shifts, $\Delta\bar{\nu}_3$ and $\Delta\bar{\nu}_4$, were considered inactive and due to symmetrical oscillations. The first two frequencies, $\Delta\bar{\nu}_1$ and $\Delta\bar{\nu}_2$, are more or less independent of the decrease of polymerization. It is concluded that the Raman spectra of the silica esters approach more and more closely that of quartz as the polymerization increases, and that this is definite evidence, therefore, of the polymerized character of the SiO_4 group as regards the crystalline and amorphous silicates. If the four fundamental frequencies attributed to the SiO_4 group are, in fact, such, then there remains a large number of lines which are present in quartz to be accounted for. This has been essayed on the basis of combination frequencies not only for those observed in Raman spectra but also in infra-red absorption spectra. There is a reasonably good agreement between twenty-seven lines observed and calculated on this basis. There are, however, some disagreements both in regard to the expected intensities and to some of the shifts actually observed in quartz.

TABLE 20

The group frequencies of SiO_4 *in silicic acid esters*

COMPOUNDS	$\Delta\bar{\nu}_1$	$\Delta\bar{\nu}_2$	$\Delta\bar{\nu}_3$	$\Delta\bar{\nu}_4$*
Monomeric ester, $SiO_4\cdot(CH_3)_4$	1205 1192 1170	1110$_w$ 1080$_w$	842$_m$	642$_s$
Dimeric ester, $Si_2O_7\cdot(CH_3)_6$	1195	1092$_w$	827$_m$	576$_m$
Trimeric ester, $Si_3O_{10}\cdot(CH_3)_8$	1190	1090$_w$	825$_m$	556$_w$
Decameric ester, $Si_{10}O_{30}\cdot(CH_3)_{22}$	1194	1086$_w$	825$_m$	518

* See footnote to table 8.

Further experiments in this direction will undoubtedly clarify these anomalies. In any case, the results are of considerable interest.

Other than silicate glasses, few amorphous compounds have been investigated in the inorganic field. A glass made from potassium alum, the product being transparent, hard, brittle, and exhibiting no x-ray pattern, was briefly examined by Hibben (125). The normal Raman shifts found in concentrated solutions of potassium alum, with the exception of $\Delta\bar{\nu}$ 982, were considerably broadened and more diffuse. The latter shift remained fairly sharp and strong. Silicate glasses of widely varying compositions have not been examined. It is not surprising that those glasses which contain silicon dioxide as a large portion of their composition should exhibit frequencies which can be more or less ascribed to the silica group.

The glasses of high index, however, contain PbO in quantities almost equal to the silica content. This would presumably result in oscillations corresponding to very small $\Delta\bar{\nu}$ not observed as yet.

SUMMARY

The Raman spectra investigation of amorphous substances is yet in its infancy. Notwithstanding certain inherent difficulties, considerable progress has been made. To interpret and evaluate the results obtained from these particular investigations requires as a preliminary a thorough and systematic study of the Raman spectra from the other states of aggregation. This has now reached a point of exactness where these results may be applied to amorphous compounds with confidence, when additional experimental data are available.

X. The Raman Spectra of Pure Liquids

The Raman spectra of pure liquids offer the advantage of high concentration; that is to say, the material to be examined consists of a single component, and any results obtained may be attributed to that component alone without the influence of ionization in solution and without the general scattering which is usually concomitant with the Raman spectra of crystals. This is particularly true of organic substances, which usually readily lend themselves to examination under these conditions. Inorganic materials, which may be examined in liquid form, are relatively rare. It may be stated, however, in general, that apart from the influence of the electrical environment, which is present in solution, the Raman spectra of liquids are consistent with the Raman spectra of the substances in the gaseous or solid state of aggregation. In some cases it is necessary to operate at a temperature of sufficient elevation that the number of molecules in the first vibrational level is not entirely negligible. This is also particularly true of the gases, as will be seen later. The zero vibrational level of the gases is usually at room temperature or considerably below. In the case of liquids, room temperature does not as a rule excite molecules above the zero vibrational level. One has in this case the advantage of increased concentration without lattice vibrations and without ionization effects. On the other hand, some of the compounds are not without color, which means that in order to register the Raman lines the exciting radiation must be of sufficiently long wave length that the Raman radiation which is emitted will not be absorbed by the medium, a process which would result otherwise in relatively increased exposure.

The results are, as a rule, confined to the halogens since these exist most readily in liquid state. Carbon tetrachloride is omitted from consideration since it perhaps more properly belongs to the category of organic compounds. At the same time, however, carbon disulfide is considered as belonging to inorganic compounds, the distinction being somewhat arbitrary. In general, as is to be expected, the principal frequencies to be obtained are four in number, from molecules of the type AX_3, the fourth fundamental frequency, according to Bhagavantam (111), coming out with relatively greater intensity than the others. Furthermore, the oscillation frequency becomes smaller with increasing atomic weight. It is interesting to note that with increasing atomic weight the interval between the third and fourth Raman frequencies continues to increase, whereas that between the first and second decreases. In the case of the compounds of the type AX_4, all the substances show four principal Raman frequencies, the third being the most prominent in every case. The results are given in table 21.

TABLE 21

Raman spectra of inorganic liquids

COMPOUND	RAMAN SHIFTS*	REFERENCES
AsCl$_3$	158_m 194_w 370_w 405_s	(235, 24, 23, 111, 227, 21, 22, 230)
AsBr$_3$	76_m 129_m 273_s	(230)
SbCl$_3$	130_s 155_m 320_m 360_s	(235, 287, 23, 24, 230)
BCl$_3$	255_m 472_m 947_w	(306)
PCl$_3$	190_s 258_s (340) 484_m 511_s (590) (1340)	(235, 24, 111, 227, 209, 270, 286, 23, 284, 21, 306, 22, 230)
PBr$_3$	116_s 162_m 380_s 400_s	(235, 24, 270, 285, 22)
POCl$_3$	192_m 268_w 338_m 485_s (583) (1290)	(291, 209, 306, 22)
SiCl$_4$	151_m 221_m 425_s 607_w	(149, 235, 111, 227, 300, 24, 15, 16, 304, 270, 22)
SiBr$_4$	90_m 137_m 249_s 487_w	(270)
SiHCl$_3$	179_m 250_m 489_s 587_m 799_m 2258_s	(305, 282, 290)
SnCl$_4$	104_m 132_m 366_s 404_m	(235, 24, 298, 111, 304, 227, 22, 291, 15, 16)
SnBr$_4$	66_w 88_m (159) 220_s 279_m	(304)
TiCl$_4$	120_m 144_w 386_s 497_m	(235, 111, 227, 304, 24, 15, 16)
CS$_2$	412 647 655_s 799_w (848) (1229) (1577)	(299, 296, 297, 288, 166, 155, 111, 227, 279, 131, 292, 295, 289, 280, 281, 307, 15, 98)
SO$_2$Cl$_2$	213_m 278_w (365) 387_m 409_s 559_m (576) 1187_m (1413)	(291, 292, 209, 22, 293)
S$_2$Cl$_2$	109_s 206_w 247 447_s (545)	(292, 209, 293, 306)
SOCl$_2$	193_s 282_m 343_s 444_w 488_m 1229_s	(292, 209, 306, 22, 293)
HgCl$_2$	314_m 376	(230)
HgBr$_2$	195	(230)

Comparing phosphorus trichloride with phosphorus oxychloride, essentially the same lines exist in both cases with the exception of $\Delta\bar{\nu}$ 511, which is absent in phosphorus oxychloride and very intense in phosphorus trichloride. Furthermore, the intensity of $\Delta\bar{\nu}$ 338 is relatively strong in phosphorus oxychloride and is just detectable in phosphorus trichloride. This may possibly be attributed in phosphorus oxychloride to phosphorus trichloride as an impurity. The line appearing at approximately $\Delta\bar{\nu}$ 1290 is attributed by Venkateswaran (306) and Nisi (209) to the P=O group. Boron trichloride gives only three detectable frequencies, although $\Delta\bar{\nu}$ 947 shows some doublet structure. Marked changes in the intensities of the Raman lines are noticed as compared with the other chlorides, the second frequency coming out more prominently.

The change in the Raman spectra of mixtures of phosphorus trichloride and phosphorus tribromide and of stannic chloride and phosphorus tribromide as a function of the relative proportion of the constituents indicating close compound formation has been mentioned in the Raman spectra of inorganic compounds (270, 271). In the compound $SiHCl_3$ $\Delta\bar{\nu}$ 2258 corresponds to an H↔Si vibration, which is appreciably less than the shift corresponding to the C↔H or S↔H vibrations and would indicate a slightly less binding force existing between the silica atom and the hydrogen atom than that between the carbon and hydrogen atoms and between the sulfur and hydrogen atoms.

The principal frequencies observed for carbon disulfide are $\Delta\bar{\nu}$ 655 and 800. The number of frequencies and their characters are connected with the fact that carbon disulfide is a linear model of the type AX_2, and is included in this discussion in order to elucidate the structure of other inorganic compounds containing sulfur. The C↔S vibration is possibly established from a study of organic compounds containing sulfur, which will be discussed in more detail in a subsequent publication. It suffices to say, that $\Delta\bar{\nu}$ 650 to 704 and $\Delta\bar{\nu}$ 740 to 805 are prominently present in mercaptans and organic sulfides (260). These lines, however, split into several components, depending upon the complexity of the structure of the remainder of the molecule. The characteristic frequency of the S↔S vibration, as is apparent in the organic disulfides, becomes $\Delta\bar{\nu}$ 512 and is entirely absent in the monosulfides. The relatively low frequency obtained for this vibration would apparently indicate a single bond binding in the case of the disulfides. On this assumption the frequency to be expected for S═S would occur at $\Delta\bar{\nu}$ 724, these two frequencies bearing the ratio of one to the other as the $\sqrt{2}$. The frequency $\Delta\bar{\nu}$ 724 is approximately that obtained from the absorption spectra of sulfur vapor. The Raman spectra of sulfur crystals and sulfur dissolved in carbon disulfide do not show this frequency, which is reasonably explicable on the grounds that under these conditions the sulfur is not present in the form of S_2, but is present in the form of a higher polymer. From the same point of view, however, it must be noted that one of the few apparent inconsistencies in this line of reasoning lies in the structure of carbon disulfide, since the frequencies characteristic of this compound, which is generally considered as S═C═S, do not vary greatly from those obtained from the mercaptans where the characteristic frequency is attributed to the C—S. It is quite evident, however, that the constitution of carbon disulfide is symmetrically arranged in regard to the sulfur atoms. On the other hand, it is not wholly impossible that the ordinary conception of the constitution of carbon disulfide may be in error. Nisi (209) has attributed $\Delta\bar{\nu}$ 1200 (approximate) to an S↔O oscillation, the frequency appearing in $SOCl_2$ and SO_2Cl_2 but being absent in S_2Cl_2. Thionyl chloride is consistent with this view. According to Venkateswaran (306), Cabannes and Rousset (22), and Matossi and Aderhold (292), the structure of this compound is $Cl_2S{=}O$. The molecule is considered by Cabannes and Rousset to have a pyramidal configuration and give rise to the six observed Raman frequencies. One of the frequencies observed occurs when the sulfur atom remains fixed and the chlorine and oxygen atoms vibrate symmetrically. Another occurs when the two chlorine atoms remain fixed and the oxygen and sulfur oscillate against each other. The third occurs when the SO group oscillates as a unit against the two chlorine atoms, which in turn vibrate along the line of the binding force against the SO group. $\Delta\bar{\nu}$ 488 represents the first of these types of oscillations, $\Delta\bar{\nu}$ 1229 the second, and $\Delta\bar{\nu}$ 193 the third. The other frequencies represent displacements transverse to the chemical bond.

The compound sulfur monochloride has the formula S_2Cl_2. This may be written in two ways, $S{=}SCl_2$ or Cl—S—S—Cl. According to Michaelis and Schifferdecker (294) and Thorpe (302, 303), the former structure is correct, analogous to thionyl chloride. On the other hand, Bruni and Amodori (283) favor the latter structure. The latter is consistent with the view of Sugden (301). The principal shifts of this compound are $\Delta\bar{\nu}$ 109, 206, 247, 447. The existence of these frequencies demonstrates that the compound cannot be, in liquid form, diatomic, that is, SCl. Venkateswaran (306) argues that the absence of a higher frequency shift above $\Delta\bar{\nu}$ 1100 and a lower frequency shift at 280 is evidence against a similarity in structure between S_2Cl_2 and $COCl_2$. More important, however, is the presence of a frequency shift near $\Delta\bar{\nu}$ 512, corresponding to S—S and the absence of a frequency near $\Delta\bar{\nu}$ 724, attributed to S=S. This is in contrast to the view of Matossi and Aderhold (292), who consider that $\Delta\bar{\nu}$ 451 is attributable to the S=S vibration and in consequence the structure is similar to thionyl chloride. This view was also held by Meyer (293). The difference in views rests in the assignment of Raman frequencies to characteristic vibrations. A determination of the Raman spectrum of sulfur vapor will possibly help clarify the matter.

SUMMARY

While the field of Raman spectra investigation in inorganic liquids is relatively small as compared with that of solutions or crystals, it has been by no means extensively studied. There is no *a priori* objection, except as a matter of experimental inconvenience, to the study of many other such compounds as those given, when in a molten state. The limiting factor is primarily a maximum temperature of approximately 450°C., wherein the black-body radiation becomes appreciable in long exposures. In general, the results are consistent with those from compounds with the constitution and configuration assigned to them. In the specific cases, ostensible disagreements with the precepts heretofore set forth are not disagreements with those precepts as such, but rather questions of interpretation. In all such cases further investigation will doubtless clarify disputed points

XI. THE RAMAN SPECTRA OF CYANOGEN COMPOUNDS

The Raman spectra of cyanides offer an interesting application of Raman spectra methods. The results, while enlightening, are not wholly satisfactory with particular regard to the sulfocyanates. The Raman frequencies are given in tabular form in table 22.

The first striking observation is the fact that the wave-number shift for the cyanogen group falls within the region which can be attributed to a triple bond rather than a double bond. Hence it may be stated that the $\mathrm{C \leftrightarrow N}$ oscillation, at least from the Raman spectra point of view, involves a triple bond. The classical method of considering the isocyanates, that is, compounds of the constitution $\mathrm{R{-}N{=}C{=}O}$, and the isothiocyanates, $\mathrm{R{-}N{=}C{=}S}$, is in the manner just given and that of the isocyanides, as $\mathrm{R{-}N{=}C}$, while the nitriles or cyanides are considered $\mathrm{R{-}C{\equiv}N}$. It is evident that this is not consistent with the Raman spectra data.

The wave-number shift near $\Delta\bar{\nu}$ 2100 is quite characteristic of all compounds containing the CN group with the possible exception of dicyanine, in which compound it is raised to a somewhat higher frequency. In hydrogen cyanide gas, this shift is $\Delta\bar{\nu}$ 2089. In hydrogen cyanide liquid, according to Bhagavantam (279), this has degenerated to a triplet. In organic compounds the shift is somewhat higher, methyl cyanide, for example, giving a shift of $\Delta\bar{\nu}$ 2246. The isothiocyanides and isocyanides are confined to organic compounds, and will not be discussed in detail here. The shifts, however, are of the same order of magnitude, but in the former compounds are generally much broader. In the cyanates the formerly accepted constitution would include a double bond for oxygen. From the Raman spectra obtained, this does not seem possible.

In spite of the complexity of the ions in some of the compounds

TABLE 22

Raman spectra of cyanogen compounds

COMPOUNDS	RAMAN SHIFTS*																REFERENCES
HCN, gas, at 80°C											2089_m						(315)
HCN, liquid										2069	2096_s^f	(2122)				3213	(312, 309, 310, 279, 315, 308, 311)
NaCN, crystalline											2085_m						(96)
KCN, solution							(838)				2081			(2160)			(316, 309, 310, 298, 318, 261, 229, 225, 263, 199)
$(CN)_2$, liquid					512	(756)	860								2334_w		(318)
$Hg(CN)_2$, solution		260_w												2196_s			(318, 261, 229, 225)
$Hg(CN)_2$, crystalline		276												2192_m			(96)
$KAg(CN)_2$, solution	239_w						855					2130_w					(96, 316, 318, 229)
$KCu(CN)_2$, solution												2110					(317)
$K_3Cu(CN)_4$, solution												2094_m	(2176)				(229, 233)
$K_2Cd(CN)_4$, solution												2142					(229, 233, 317)
$K_4Fe(CN)_6 \cdot 3H_2O$, crystalline													2161				(96)
$K_4Fe(CN)_6$, solution										2051_m	2092_m		2153	2195			(233)
$K_2Ni(CN)_4$, solution												2144_m					(268)
$K_2Ni(CN)_3(?)$, solution												2142_m					(268)
$K_2Hg(CN)_4$, solution													2150_m				(229, 317)
$K_2Zn(CN)_4$, solution										(2055)			2149_m				(317, 233)
$K_3Cr(CN)_6$, solution						782						(2137)					(233)
$K_4Cr(CN)_6$, solution						619						2130					(268)
$K_3Co(CN)_6$, solution			340_m	(405)						(2070)		2141_m					(233, 268)
$K_4Ru(CN)_6$, solution			381							2068		2107					(268)
$K_3Rh(CN)_6$, solution					593							2145_m					(268)
NaSCN, solution						754_w				2076_m							(313, 314, 319)
KSCN, solution						747_m				2058_s							(313, 314, 316, 318, 96)
KSCN, crystalline						747_m				2050_s							(96)
NH_4SCN, solution						744_m				2066_s							(313, 314, 316, 96)
NH_4SCN, crystalline										2067_m							(96)
$Ba(SCN)_2$, crystalline						776				2053_m							(96)
KOCN							838_w	1229	1314					2183_w			(316)
ClCN			397_w			729_m								2201_s			(323)
BrCN			368_w		580_m									2187_s			(323)
ICN			321	470_m								2158_s					(323)

given, relatively few Raman shifts are observable. $\Delta\bar{\nu}$ 782 for $K_3Cr(CN)_6$ and $\Delta\bar{\nu}$ 340 for $K_3Co(CN)_6$ have been attributed to the oscillation of the complex (233). The same might be said of $\Delta\bar{\nu}$ 855, observed in $KAg(CN)_2$. The shift $\Delta\bar{\nu}$ 838 possibly observed in potassium cyanide solution (316) is doubtful. Otherwise, the shifts appearing near $\Delta\bar{\nu}$ 750 appear exclusively in those compounds containing sulfur, and are attributed to the triatomic nature of the ion. This may also be said of the shift $\Delta\bar{\nu}$ 838 observed in potassium cyanate (316). Otherwise, there is present a somewhat curious anomaly, namely, the compounds containing heavy cations have larger frequency shifts than those compounds which contain lighter ones. · This is diametrically opposed to observations with other compounds, and has been explained by Pal and Sen Gupta (317) as due to a change in the binding force which is influenced by the electronic configuration surrounding the atom. Krishnamurti (96) attributes $\Delta\bar{\nu}$ 260 and 276 in mercuric cyanide (solution or crystalline) to the Hg↔CN oscillation, and considers the molecule as linear, the binding force being mainly homopolar. The larger frequency shift ($\Delta\bar{\nu}$ 2100) is greater with an increase in the homopolar nature of the R—CN binding. The same view is taken by Samuel and Kahn (268). In the thiocyanates the decrease in the CN shift is attributed by Krishnamurti to the influence of a double bond between the sulfur and the carbon atom, the carbon being supposed to be joined to the nitrogen by a double bond in the classical manner. $\Delta\bar{\nu}$ 747 is considered characteristic of S═C. This view does not seem to be particularly tenable, first because the magnitude of the frequency shift corresponding to the C↔N oscillation is greater than that to be expected from a double bond linkage; second, this shift is not radically different from that ascribed by Krishnamurti to the triply bonded CN linkage in other compounds; and last, $\Delta\bar{\nu}$ 747, ascribed to an S═C oscillation, is quite close to the C—S oscillation observed in mercaptans and methyl sulfides. The latter difficulty has been mentioned in discussing the shifts observed in carbon disulfide. If the assumption as to the nature of the triple bond between carbon and nitrogen is correct, which seems probable, then the constitution of the thiocarbimides can only involve a single bond between the carbon and sulfur. There are two lines which fall within this region, namely $\Delta\bar{\nu}$ 645 (s) and $\Delta\bar{\nu}$ 796 (w) in ethyl thiocarbimide (309, 310).

Dadieu and Kohlrausch (193) presume a ring structure between the nitrogen, carbon, and sulfur atoms which would account both for the triple bond between the carbon and nitrogen and for the single bond between the carbon and sulfur in these compounds. The triple bond in the cyanogen group and isonitrile is also assumed by Sugden (322). He does, however, assume a double bond between the carbon and sulfur in the thiocarbimides on the basis of the parachor. In this case, however, he is not able to distinguish between the constitution N≡C—S and N=C=S, the two giving identical results (321). The difficulty is that the C—S oscillation varies over some seventy wave numbers, coupled with the fact that the generally accepted constitution of carbon disulfide falls within approximately the same range. While the latter is supposed to have no electric moment and consequently is presumably linear (320), a ring structure in this compound would make compatible all of these data. It remains to be seen what further investigations will provide to clarify this point.

There is no apparent reason why the shifts observed for a solution of potassium ferrocyanide should be appreciably less than that observed in the crystal—or at least it is not clear why there is a difference of the magnitude indicated.

The constitution of the cyanides and the isonitriles is fairly conclusively demonstrated by these Raman spectra investigations. This differs from the constitution formerly assumed for these compounds. The constitution of the isothiocyanates or thiocarbimides is not quite as clearly defined. The isocyanates, on the other hand, would indicate the absence of a double bonded oxygen and the presence of a triple bond between the carbon and nitrogen. The triple bond structure of the cyanides is likewise supported by the work of West and Farnsworth (323), who have investigated the cyanogen halides both in liquid state and in alcoholic solution. For each halogen derivative three frequency shifts were observed, each, in descending order, depending upon the mass of the substituent halogen. The molecule is considered linear, and it is concluded that the magnitude of the carbon–nitrogen linkage remains relatively constant, while the valence force joining the halogen to the carbon steadily decreases in the order of chlorine, bromine and iodine.

XII. The Raman Spectra of Gases

The Raman spectra of gases have been reserved for final consideration, first because gases have been partially discussed in the section on "Theory," and second because their spectra are of perhaps more interest to the physicist than to the chemist. Inseparable from this discussion are the Raman spectra of gases in the solid states of aggregation and in solution, where the solubility of the gas is sufficient to make the latter investigation possible.

There are essentially three types of Raman lines occurring in gases: first, those which are purely rotational Raman spectra and which may also occur in the liquid state; second, vibrational Raman spectra, which are of the type which has been dealt with almost exclusively up to this point; and, third, rotational-vibrational Raman spectra, which occur when the vibrational quantum number changes and superimposed on this is also a change in the rotational quantum number. In table 23 are given the *vibrational* Raman spectra of the gases, liquids, and solids for those compounds which generally occur in a gaseous state.

In the case of hydrogen and carbon disulfide there are included in the table some of the vibrational-rotational Raman spectra. Diatomic molecules, such as hydrogen, oxygen, and nitrogen have only one Raman line corresponding to a transition from the zero to the first vibrational level. In the case of oxygen and nitrogen in a liquid state, however, two lines appear which doubtless have been clearly explained by Rasetti (359) as due to the absorption of two quanta of incident radiation, the shifts $\Delta\bar{\nu}$ 3085 and $\Delta\bar{\nu}$ 4633 being almost exact multiples of the primary quantum transition, corresponding to $\Delta\bar{\nu}$ 1552 and $\Delta\bar{\nu}$ 2330. Rotational transitions have been observed for hydrogen, nitrogen, carbon dioxide, ammonia, and hydrogen chloride. Other gases show evidence of rotational effects sometimes characterized as "wings," which are imposed upon the vibrational shifts, but which cannot as a rule be re-

TABLE 23

Raman spectra of compounds generally occurring in a gaseous state

COMPOUNDS	RAMAN SHIFTS*												REFERENCES
H_2, gas	4125	4143_{w}	4158_{s}	4162	4714								(362, 360, 165, 332, 330, 83, 333, 336, 58)
H_2, liquid			4158_{s}										(351, 350, 352, 97, 354, 349)
O_2, gas		1556_{s}											(362, 360, 329, 331, 83, 369, 58)
O_2, liquid		1552_{s}	3085										(350, 352, 351, 349)
O_3, gas	1280_{w}												(370)
N_2, gas	2331_{s}												(362, 360, 329, 331, 83, 58)
N_2, liquid	2330_{s}	4633											(363, 352, 351, 349)
CO_2, gas	1241	1265_{w}	1286_{m}	1305	1325	1344	1369	1389_{s}	1409_{w}	1433			(341, 329, 361, 83, 344, 345, 347, 353, 58)
CO_2, liquid			1283_{m}					1387_{s}	1412_{w}				(335, 353)
CO_2, solid			1285_{m}					1388_{s}					(353)
CO, gas							2146_{w}						(361, 363, 364, 334)
COS	524	(678)	859_{s}	1041	1383	2055			2233				(232)
NH_3, gas		(934)	(964)				(1922)	(2110)	(2270)		3334_{s}		(341, 104, 372, 324, 325)
NH_3, solution				1073		(1615)				3221_{m}	3310_{m}	3390	(116, 343, 365, 233, 371, 346)
NH_3, liquid (room temperature)				1070	1594					3212_{w}	3300_{s}	3384	(341, 111, 226, 227, 232, 340, 289)
NH_3, liquid (low temperature)				1070	1580					3210_{m}	3310_{m}	3380_{m}	(287, 24)
N_2O, gas		1170	(1185)	1260	1284_{s}		1315	2210	2224_{w}				(341, 329, 347, 83, 327, 348)
N_2O, liquid					1281_{s}				2223_{w}				(355, 341)
$(NO_2)_2$, at −80°C		275_{m}											(356)
NO		1877											(362, 360, 334, 101)
H_2O, vapor		(984)	1648	3654									(62, 169, 180)
H_2S, gas		2615_{m}											(328, 83)
H_2S, liquid	2578_{m}												(328, 232)

SO_2, gas	1154_s	(279, 83)
SO_2, solution	1136_s	(202)
SO_2, liquid	526 1145_s 1334_m 1340	(197, 111, 227, 209, 232, 292)
SO_3, liquid	535_m 1068_s 1403_m	(226, 227, 12)
S_2O_6, liquid	290_m 370_s 666_w 697_w 1271_s 1489_w	(226)
HCl, gas	2880_m	(373, 374, 372, 222)
HCl, liquid	2778_m	(366, 340, 216)
HCl, solid	2760	(365a)
HBr, gas	2558_w	(367, 368)
HBr, liquid	2487	(367, 368)
HBr, solid	2465	(365a)
HI, gas	2233_w	(367, 368)
Cl_2, liquid	556_s	(111, 337, 339)

* See footnote to table 8.

solved into definite lines. On account of the low concentration of scattering material, the determination of the Raman spectra of gases is difficult. This has been partially solved by increasing the pressure, but as will be seen later, apart from physical imitations, the rotational transitions will not appear when the pressure exceeds certain critical limits.

In table 24 are given the Raman spectra of hydrogen liquid as determined by McLennan, Smith, and Wilhelm (97), and the transitions observed in hydrogen gas by Rasetti (360). The strongest line is that which corresponds to the transition from the zero vibrational to the first vibrational level, $\Delta\bar{\nu}$ 4156. The shifts $\Delta\bar{\nu}$ 354, 587, 814, and 1034 are rotational transitions occurring in the zero vibrational level and correspond to a change in the rotational quantum number in units of two, two of the lines occurring as anti-Stokes lines. The shifts occurring above $\Delta\bar{\nu}$ 4156 are changes in the rotational quantum number concomitant with a shift in the vibrational quantum number 0 to 1, as indicated.

In the liquid the resolution was not sufficient to determine whether the transition corresponding to $\Delta\bar{\nu}$ 4156 corresponded to the $0 \rightarrow 0$ or $1 \rightarrow 1$ rotational level.

McLennan, Smith, and Wilhelm (97) have been able to follow the conversion of ortho- to para-hydrogen by means of changes in intensity of the rotational Raman spectra as a function of time. The $0 \rightarrow 2$ transition doubles in intensity in two days' time, while the $1 \rightarrow 3$ transition decreases in intensity relative to $0 \rightarrow 2$. In other words, $\Delta\bar{\nu}$ 587 decreases and $\Delta\bar{\nu}$ 354 increases in their relative intensities in liquid hydrogen during the first forty-eight hours after preparation.

While some rotational spectra have been noted for oxygen by Rasetti (58), nitrogen gives much better results. The results seem to support the hypothesis that in a normal state only even rotational levels are present, or at least that they have a higher statistical weight than the odd ones. The spacing of the lines corresponding to $\Delta\bar{\nu}$ 16 and the transitions observed occur between $\Delta j = 6$ to $\Delta j = 16$ in steps of $\Delta j = \pm 2$.

Rotational transitions in the zero vibrational level for carbon dioxide have been observed by Houston and Lewis (345). The

$\Delta\bar{\nu}$ observed occur between 11.6 and 55.5, advancing in increments corresponding to $\Delta\bar{\nu}$ 3, a total of fifteen lines being registered. These correspond to changes in the rotational quantum number, beginning with $\Delta j = \pm 2$. From these values the moment of inertia, $I = 70.2 \times 10^{-40}$ g. cm.^{2} is calculable. It was originally supposed that some of the vibrational Raman spectra represented combination scattering (361), but more recently $\Delta\bar{\nu}$ 1289 is presumed to owe its origin to the inactive frequency, $\Delta\bar{\nu}$ 1274, calculated by Eucken (342) for a linear model of carbon dioxide.

TABLE 24

MOLECULAR TRANSITIONS OBSERVED IN H_2 GAS			MOLECULAR TRANSITIONS OBSERVED IN H_2 LIQUID		
n	Δj	$\Delta\bar{\nu}$	n	Δj	$\Delta\bar{\nu}$
0→0	3→1	−587.3			
	2→0	−354.5	0→0	2→0	−351
	0→2	354.1		0→2	356
	1→3	587.5		1→3	587
	2→4	814.4			
	3→5	1034.6			
0→1	0→0	4162.1	0→1	0→0	4156
	1→1	4156.0		1→1	
	2→2	4144.8			
	3→3	4126.9			
	0→2	4498.4			
	1→3	4713.3			
	2→4	4917.8			
	3→5	5109.8			
	2→0	3807.4			
	3→1	3568.9			

The magnitude of the vibrational frequency shift for carbon monoxide as observed by Rasetti (361) and Bhagavantam (334), namely, $\Delta\bar{\nu}$ 2146, is indicative of the triple-bonded nature of the union between carbon and oxygen in this gas.

The Raman spectrum of ammonia has been investigated extensively. There are essentially three strong maxima in the liquids and in solution. These are, however, somewhat broad and diffuse and are somewhat reminiscent of the water bands.

In gaseous ammonia the central shift, $\Delta\bar{\nu}$ 3334, is reasonably sharp. Two lower frequency oscillations at $\Delta\bar{\nu}$ 934 and 964 have been observed by Amaldi and Placzek (324, 325). The three frequency shifts between $\Delta\bar{\nu}$ 1922 and 2270, also observed, are questionable. Rotational Raman spectra for ammonia gas have also been observed (325). The rotational $\Delta\bar{\nu}$ obtained are $\Delta\bar{\nu}$ 79, 99, 119, 140, 159, 179, 199, 219, 258, 298, and 336, as both Stokes and anti-Stokes lines. These correspond to transitions in which the rotational quantum number Δj changes by ± 1 as well as ± 2 and 0, which is compatible with the non-linear character of the molecule. Langseth (346) has analyzed the fine structure of the ammonium bands in concentrated solutions of ammonia and observed thirty-two lines occurring between $\Delta\bar{\nu}$ 3022 and $\Delta\bar{\nu}$ 3661, corresponding to the rotational-vibrational transitions in which the rotational quantum number changes by ± 1 or ± 2, corresponding to the *O S* and *P R* branches, the *Q* branch being represented by the shift $\Delta\bar{\nu}$ 3312. This leads to a calculated moment of inertia of 2.8×10^{-40} g. cm.^{2} for the molecule (346, 371).

It has been suggested that there may be some evidence of association of the ammonia molecule in liquid form (326, 338). This view was also held by Bhagavantam (226). It is predicated on a change in the relative intensities of the three higher frequency shifts with increasing temperature, $\Delta\bar{\nu}$ 3384 and 3212, becoming more feeble with an elevation in temperature. The shifts occurring at $\Delta\bar{\nu}$ 1070 and 1594 remain relatively constant and are attributed to characteristic oscillations of the ammonia molecule itself.

Aqueous solutions of ammonia give a Raman spectrum identical with that of the liquid itself. Investigations of solutions at various concentrations by Hollaender and Williams (343) and by Ricca (365), for example, show no evidence of the presence of an NH_4 ion as such. Aqueous solutions of ammonium salts, such as ammonium nitrate and ammonium chloride, show no Raman lines attributable to the NH_4 ion.

Two prominent frequency shifts are observed for nitrous oxide, $\Delta\bar{\nu}$ 1284 and 2224. The first of these is the stronger and is presumably attributable to a symmetrical oscillation. The remaining shifts indicated in table 23 are very faint. From these Langseth and Nielsen (348) calculate a moment of inertia of 61 × 10^{-40} g. cm.^{2} The structure of the molecule is linear and unsymmetrical, $\Delta\bar{\nu}$ 1284 corresponding to the oscillation $\overrightarrow{N}\ N\ \overleftarrow{O}$ and $\Delta\bar{\nu}$ 2224 to the oscillation $\overrightarrow{N}\ \overleftarrow{N}\ \overrightarrow{O}$ (327). The magnitude of the frequency shift would indicate the presence of a triple bond, and not the structure $N{=}N{=}O$ as it was formerly written. From a consideration of interatomic distances and moments of inertia of the molecule Pauling (357, 358) has recently come to the conclusion that the molecule resonates between several structures but that the effective binding over any period is $N{\equiv}N{=}O$. A similar resonance was also postulated for carbon monoxide, the triply bonded structure predominating.

Nitrogen peroxide (N_2O_4) has been included at this point because of its similar chemical composition to the other oxides of nitrogen. Menzies and Pringle (356) have observed $\Delta\bar{\nu}$ 275, which is considered an inactive fundamental. It is argued that if the molecule is linear, as presumed from x-ray analysis of NO_2 at -80°C., the first vibration would be a symmetrical oscillation of the oxygen atoms about the stationary nitrogen atom analogous to that observed with nitrous oxide, and a faint line should be present corresponding to the unsymmetrical oscillation, both shifts being not greatly removed from those observed with nitrous oxide. No such lines were observed.

Not much can be said at this time regarding ozone or nitric oxide. Sutherland and Gerhard (370) have observed in ozone a very weak doublet corresponding to a mean frequency shift of $\Delta\bar{\nu}$ 1280. The weakness of the Raman spectrum is evidence against any simple symmetrical structure and suggests a non-equilateral triangular form of the molecule. Bhagavantam (334) has observed $\Delta\bar{\nu}$ 1877 in nitric oxide together with some unresolved rotational wings. Rasetti (101) has calculated the rotational transitions in nitric oxide.

Dadieu and Kohlrausch (232) have systematically investigated sulfur dioxide, hydrogen sulfide, and carbonyl sulfide, with the results given in table 25.

The frequency shifts from which these calculations may be made are given in table 23. The molecule, COS, is linear and unsymmetrical. The molecules SO_2 and H_2S are non-linear. The molecules CS_2 and CO_2 are both linear and symmetrical.

It might be mentioned that hydrogen sulfide shows a more marked change in its Raman shift in passing from the liquid to the gaseous state of aggregation than most substances. This difference is from $\Delta\bar{\nu}$ 2578 to $\Delta\bar{\nu}$ 2615. In most other compounds, where association plays no obvious rôle, the shifts are within a few wave numbers of each other in solid, liquid, or gaseous states where such data are available.

TABLE 25

Molecular constants calculated from the Raman effect

SUBSTANCE	α	$s \times 10^8$	$F \times 10^{-5}$	$d \times 10^{-5}$
		cm.	*dynes per cm.*	*dynes per cm.*
$\mathrm{O{=}C{=}O}$	180°	0.98	13.7	1.2
$\mathrm{S{=}C{=}S}$	180°	—	6.9 (ca.)	1.5 (?)
$\mathrm{O{=}C{=}S}$	180°	O...C 1.04 C...S 2.38	13.6 8.0	0.4
$\mathrm{O{=}S{=}O}$	120°	2.24	9.6	1.6
$\mathrm{H{-}S{-}H}$	90°	1.43	3.9	0.02
$\mathrm{S{-}H}$	—	1.35	3.8	—

α = valence angle; s = interatomic distance from central atom; F = force constant in dynes per centimeter; d = deformation constant in dynes per centimeter.

The polymerization of sulfur trioxide and the absence of any Raman effect in aqueous solutions of hydrogen chloride have already been pointed out. As is to be expected, both liquid and gaseous hydrogen chloride have frequency shifts indicative of the homopolar nature of the binding under these conditions. This transition corresponds to the Q branch.

A series of experiments carried out by Bhagavantam (227, 83) on the effect of pressure on the rotational and vibrational Raman spectra of gases has led to interesting observations. It is presumed that the influence of neighboring molecules on Raman spectra may be attributed partly to a general intermolecular field and partly to collisions. The mean frequency of collisions is a function of the pressure and the viscosity of the medium. As long as the pressure/viscosity ratio $(P\eta)$ is small the perturbing influence of collisions on molecular rotation is small. By taking P/η to be equal to the frequency of rotation of the molecule in the one quantum state an estimate can be made of the pressures at which complete rotational quantization will no longer clearly exist. These can then be compared with the observed pressures at which discrete lines in the rotational Raman spectra fade and tend to become continuous. The observations yield the following results, the pressure being given in atmospheres:

	Calculated	*Observed*
Oxygen	25	20–30
Nitrogen	29	30
Carbon dioxide	5	5

In some cases the observed rotational spectra diminish at pressures lower than the calculated pressure, and are attributed to the action of intermolecular fields.

Braune and Engelbrecht (230) have investigated a number of inorganic halides in the gaseous phase and compared the frequency shifts so obtained with those observable in liquid phase and in solution. The results in $\Delta\tilde{\nu}$ are shown in table 26.

TABLE 26

HALIDE	$\Delta\tilde{\nu}$		
	(gas)	(solution)	(liquid)
$HgCl_2$	355	331	314
$HgBr_2$	220	205	195
PCl_3	523		511
$AsCl_3$	422		405
$SbCl_3$	382		360
$AsBr_3$	287		273

The frequency shifts observed in the gaseous state are greater in every case than the equivalent shift in the liquid, and this is attributed either to an increase in the binding forces through the action of adjacent molecules or to a decrease in the oscillating mass on vaporization. With stannic chloride, however, two shifts are observed in the gas, $\Delta\bar{\nu}$ 367 and $\Delta\bar{\nu}$ 400, both closely corresponding to the shifts observed in the liquid. The percentage differences in the frequencies in the vapor and liquid states are approximately a linear function of the dipole moment. This is indicated in figure 17, where these differences are plotted against the observed and calculated moments. It is also observed that the inactive oscillation of the mercuric halides in the vapor state is proportional to their heat of dissociation.

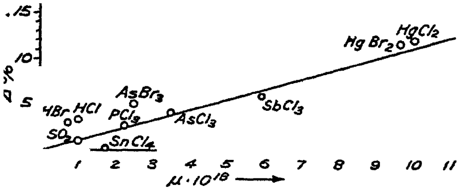

FIG. 17. PER CENT DIFFERENCE BETWEEN THE VAPOR AND LIQUID RAMAN SPECTRA OF SOME INORGANIC HALIDES PLOTTED AGAINST THE CALCULATED AND OBSERVED MOMENTS OF THESE COMPOUNDS (After Braune and Engelbrecht)

XIII. CONCLUSION

It has been the purpose of this review to outline the interpretation, the development, and the application of Raman spectra, to collect, and to a certain extent to analyze, the data upon which such interpretations and applications are predicated. There are many fields which have not been explored. There are others which need further investigation. There are some contradictions and discrepancies. The contribution already made, however, to physics and chemistry by Raman spectra investigations is undisputed. The enormous progress already made in the five years since this discovery was announced speaks more eloquently than words as to its future utility.

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BIOGENETICS IN THE TERPENE SERIES

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INTRODUCTION

Attempts to explain the biogenesis of the terpenes on the basis of occurrence side by side in one or more species of plants have not been wanting, but no scheme that is wholly satisfactory has appeared. The following explanation, which is based upon the chemical composition of all known terpene-containing volatile oils that occur naturally in the plant kingdom, departs somewhat from the usual conception. In consequence, many exceptions to the tentative rules that it advances will doubtless be found, especially since the study deals with general tendencies in the plant kingdom rather than with general laws.

Robinson (6) has developed a concept—state of oxidation (S.O.)—which, when applied to plant products, should serve as an important guide in biogenetic reasoning. State of oxidation is defined as the "number of hydroxyl groups present in the saturated open-chain formula of the substance, the saturation and ring fission being brought about by the addition of water."

As early as 1906 Semmler (7) suggested that the volatile oils were necessarily regressive products of metabolism and that the processes of dehydration, oxidation, and reduction as the plant applies them to sugars can explain the formation of the volatile oils.

Assuming that the formation of the volatile oils, as well as the genetically related phenols, methylated phenols, and those of their derivatives that do not happen to be volatile with steam, is by the condensation of simpler units produced in sugar metabolism in the plant, it is evident that the state of oxidation of the resultant compounds may then depend upon the degree to which the sugars are reduced or oxidized in metabolism. The resultant compounds, such as terpenes and allyl- and propenyl-phenols, may be formed from the same source material, although by slightly different routes that are unlike principally in the degree of oxidation of the simpler units from which they are finally formed.

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[1] Maintained at Madison, Wisconsin, in coöperation with the University of Wisconsin.

In consequence, the application of logical reasoning to the biogenesis of volatile compounds will probably be more successful if it is limited to compounds in the same state of oxidation, unless there is excellent reason to think that a compound in a higher state of oxidation is derived in the plant directly from one in a lower state of oxidation, as piperitone is derived from piperitol. This discussion will therefore be confined to the biogenetic derivation of substances referable directly to the terpenes, $C_{10}H_{16}$, S.O.3.

The possible derivation of terpenes and their relatives by the aldol and true condensation of acetaldehyde and acetone has been taught by Edward Kremers for probably forty years, but he does not believe the idea originated with him. Smedley (11) suggested that citral was formed in the plant from two molecules of acetone and two of acetaldehyde. R. E. Kremers (4) amplified this theory in applying it to the mints. He indicated the derivation of the terpenes by way of citral, the latter being reduced at a double bond to form the precursor of the menthol series, citronellal. Astengo (1) regards isovaleraldehyde as the common progenitor of the entire group of compounds. The ideas of Kremers and Astengo were amplified by Francesconi (2).

Read (5) presents a most interesting theory relating many terpenes and terpene alcohols to geraniol. Taking his clue from the occurrence of geraniol in many eucalyptus oils, he is able to show the derivation in somewhat logical fashion of piperitol, piperitone, phellandrene, terpinenol-4, the carenes, α-terpineol, cineole, and pinene. His reasoning is based partly upon the occurrence of related compounds in the same oils.

Read's theory is recorded by Simonsen (9), with a tabulation placing piperitol, piperitone, 1,3-dihydroxymenthane and the phellandrenes in one group, terpinenol-4, terpinolene, 1,4-cineole, and sabinene in a second, and the Δ^4-carene in a third. Simonsen indicates that all these are derived in the plant from geraniol by simple means.

The derivation of all the terpenes from geraniol requires a shifting of double bonds and the formation of inner rings by successive hydrations and dehydrations in the plant analogous to similar processes performed *in vitro*. The straightforward cyclization of geraniol gives rise only to terpinolene, and considerable rearrangement must take place to arrive at the other members of the terpene group. Assuming that phytochemical processes are rather direct in their aim, it seems more logical to attempt to refer all known terpene configurations to underlying fully hydroxylated compounds. The simple dehydration of such compounds in a single stage, that is, without supposing any rehydration, should give groups of hydrocarbons of related biogenetic characteristics. The relationships found in such a derivation should persist in a more or less consistent fashion throughout all known volatile oils.

Corollaries to the preceding deductions are the assumptions that the terpenes as they occur in the plant represent true end products of metabolism, that is, are not mutually transformable in the plant except in certain restricted instances, and that, even in such instances, the transformation probably proceeds in one direction only. The configurations of the final products, the terpenes, are established by the configurations of their acyclic progenitors. In turn, the configurations of these perhaps transitory substances are established by the manner in which the simple metabolic products of the sugars are condensed in the plant. The state of oxidation of these simple products will determine to a large degree the state of oxidation of the resultant compounds.

Any phytochemical generalizations limited to data obtained from a species, a genus, or even a family are questionable. The coëxistence of compounds in a few instances out of many, for example, may indicate nothing as to their biogenetic relationship; their coëxistence in a large percentage of their occurrences may indicate, not so much their mutual transformation one into the other, as their derivation from a common source.

DERIVATION OF GROUPS

In order to arrive at the possible precursors of the terpenes, it is convenient to deal with geraniol, which occurs in nature with

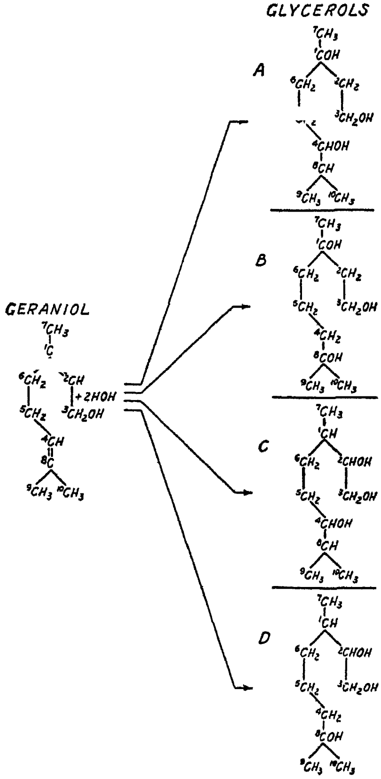

Fig. 1. The Derivation of Four Glycerols from Geraniol

all known types of the terpenes. For convenience geraniol is written in figure 1 in a form for cyclization, and the carbon atoms are numbered in cyclic manner. The addition of the elements of two molecules of water in simple fashion indicates that geraniol may have arisen in nature by the dehydration of four different glycerols,—A, B, C, and D. If geraniol had been written in the "limonene" manner, that is, Δ^8, it would have arisen from only the second and fourth of the glycerols, omitting the important first glycerol. These glycerols can be cyclized by the elimination of one molecule of water, as in figure 2. From each of the six cyclic glycols or menthanediols obtained in this fashion, the derivation of the terpenes, related alcohols, and the oxides may be started by simply eliminating one or two molecules of water in logically conceivable ways, as indicated in figures 3 to 8, inclusive. In these diagrams the compounds found in nature are underscored.

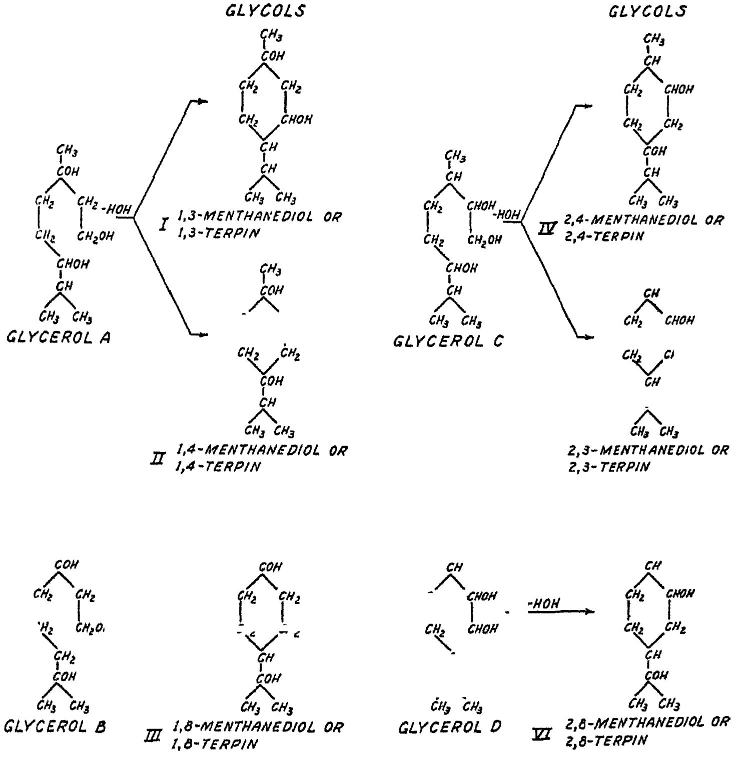
GLYCOLS
GLYCOLS
-HOH
-HOH
-HOH
GLYCEROL A
GLYCEROL C
I 1,3-MENTHANEDIOL OR 1,3-TERPIN
II 1,4-MENTHANEDIOL OR 1,4-TERPIN
IV 2,4-MENTHANEDIOL OR 2,4-TERPIN
2,3-MENTHANEDIOL OR 2,3-TERPIN
GLYCEROL B
III 1,8-MENTHANEDIOL OR 1,8-TERPIN
GLYCEROL D
VI 2,8-MENTHANEDIOL OR 2,8-TERPIN

FIG. 2. THE CYCLIZATION OF FOUR GLYCEROLS

The compounds arranged under the respective glycols exhibit certain characteristics of association that furnish a working basis for testing the entire hypothesis. It seems logical that, if the development indicated is in line with the development actually transpiring in the plant, the same associations observed in the groups outlined should persist in the plant kingdom. Oils consisting entirely of representatives of one group, however, might be expected to be very rare. Thus, piperitol, piperitone, and the phellandrenes are found only under glycol I. Glycol II produces sabinene, which occurs in no other series. Glycol III has 1,8-cineole and β-pinene exclusively. Glycol IV shows thujyl alcohol. Glycol V furnishes no special arrangement. Glycol VI gives dihydrocarveol and borneol.

An examination of all recorded occurrences of these substances should give some indication of the validity of the scheme, although, of course, any conclusions drawn can be no more valid than the data upon which they are based. In the following compilations, therefore, care has been taken to eliminate from consideration instances of doubtful occurrence. Where distinct oils were reported from separate parts of a plant, as, for example, an oleoresin and a leaf oil, each oil was recorded separately. Liberal use has been made of the new edition of Wehmer (12), of Gildemeister and Hoffman (3), and of the recent issues of the annual reports of Schimmel and Company. Reference to the original was made when a doubtful point of importance arose.

Glycol I

Read (5) has noted and discussed the association of piperitol, piperitone, and the phellandrenes in the plant kingdom. Generally, in reporting the occurrence of a phellandrene, authors do not say which modification is present, but, for the present purpose, this really makes no difference because phellandrenes, piperitol, and piperitone do not occur in any other series.

Piperitol has been reported in five species of *Eucalyptus*. In four of these, either phellandrene, piperitone, or both, accompany it. In three of these it is accompanied by phellandrene, in three by piperitone, and in two by both. Simonsen (8) reports it in a species of *Andropogon* associated with d-Δ^4-carene, the formation of which from piperitol or glycol I requires elimination of water between carbon atoms 3 and 8 (figure 3). Or, carrying it back to the underlying glycerol, we can dehydrate first between carbon atoms 3 and 8, forming a seven-membered ring, and then between 3 and 4, forming the six-membered ring (figure 4).

In short, whether we start from piperitol, the glycol, or the glycerol, the carenes can be derived from the same parent substance as the phellandrenes, although they must take a little different route. The carenes occur again under glycols III and VI, and the Δ^4 variety under glycol V.

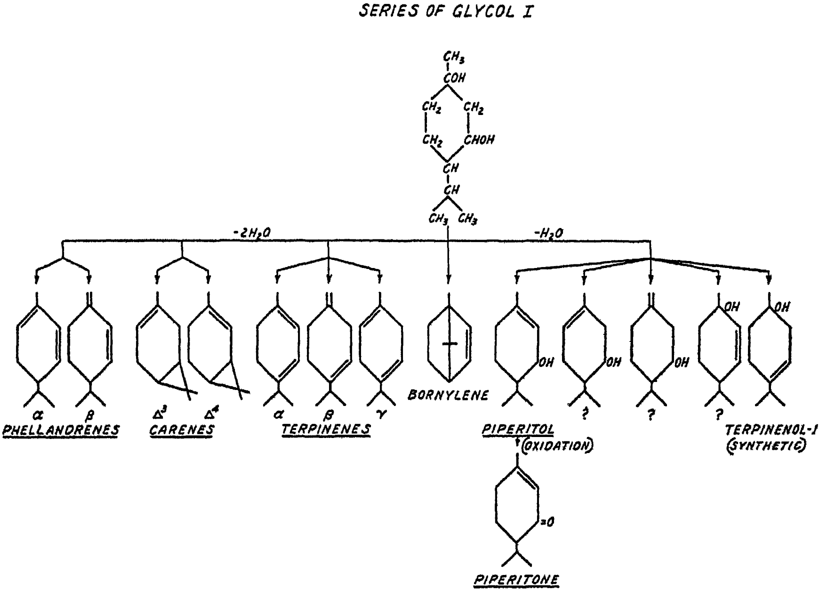

Fig. 3. The Series of Compounds Possibly Formed from Glycol I by Eliminating Water

We may consider piperitone a direct oxidation product of piperitol and, as such, it should occur in conjunction with phellandrenes as well. As a matter of fact, it is reported twenty-three times, eighteen of which are in the *Eucalyptus* genus. Of these eighteen eucalyptus oils containing piperitone, sixteen contain also phellandrene. Of the other five oils, *Cymbopogon schoenanthus* also contains piperitone and phellandrene. The fact of their joint occurrence in oil of *Mentha piperita* grown at Madison, Wisconsin, is not definitely established. One oil, that of *Mentha arvensis*, is not reported as containing compounds accompanying piperitone. *Andropogon iwarancusa* contains Δ^3-carene, to which the same reasoning applies as to the *Andropogon* already discussed. The remaining oil, *Mentha pulegium*, contains pulegone, the formula of which does not fit into the present scheme.

The close association in occurrence between piperitol, piperitone, phellandrenes, and, in a small way, the carenes, leads to the thought that they may be derived in the plant from a common progenitor. The specificity of this association in the series of glycol I (see figure 3) lends weight to the assumption of such a progenitor substance.

The phellandrenes, α or β, or both, are reported as occurring one hundred and twenty-six times, fifty-five in the eucalypts and seventy-one in non-eucalypts. Thirty-eight of these oils may be considered as typically phellandrene oils, that is, the phellandrenes, piperitol, or piperitone form the major portion of the oil. Twenty-eight of these thirty-eight instances, however, are eucalypts, leaving only ten predominantly phellandrene oils out of eighty-eight, exclusive of the eucalypts.

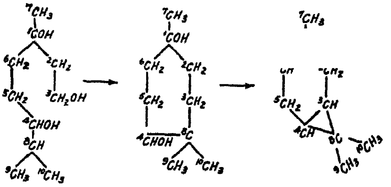

Fig. 4. The Derivation of the Carenes

Table 1 shows the occurrences of the phellandrenes with other substances.

Peculiar to the genus *Eucalyptus* seems to be the formation of phellandrene oils with a wide association of pinene and cineole, but containing neither limonene nor terpinenes. Outside of this genus, however, the association of pinene and limonene with phellandrene is especially wide.

Glycol II

The series of glycol II (see figure 5), derived from the same glycerol as the glycol I yielding the phellandrene series, contains all the terpinenes, although in association with terpinenol-4 and sabinene. To follow the occurrences of terpinenol-4 and especially sabinene, which incidentally is specific to the series, should be of interest.

TABLE 1

The reported occurrence of the phellandrenes in association with other substances

ACCOMPANYING COMPOUND	EUCALYPTS	NON-EUCALYPTS	TOTAL IN 126 OILS CONTAINING PHELLANDRENE
Pinene α β	31	35	66
Cineole	49	16	65
Limonene or dipentene	0	27	27
Piperitone or piperitol	16	4	20
Terpinenes	0	5	5

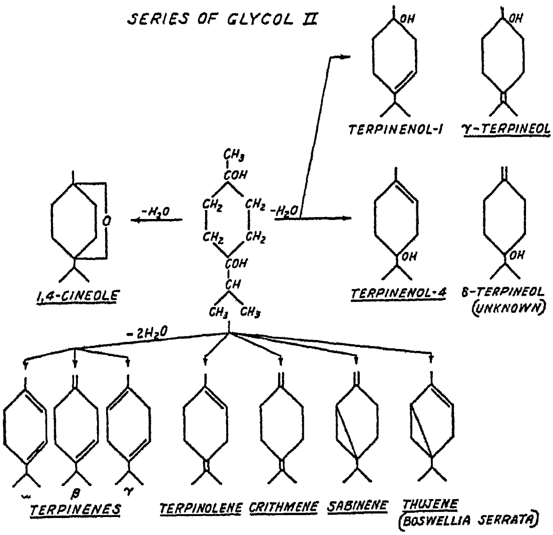

FIG. 5. THE SERIES OF COMPOUNDS POSSIBLY FORMED FROM GLYCOL II BY ELIMINATING WATER

Sabinene is reported as definitely established in sixteen oils, and of doubtful occurrence in seven others. Those in which it may be considered as established are *Juniperus communis, Juni-*

perus sabina, *Cupressus torulosa*, *Thuja plicata*, *Thuja occidentalis*, *Elettaria cardamomum var. major*, *Piper cubeba*, *Pilea* (species unknown), *Cinnamomum kanahirai*, *Xanthoxylum rhetsa*, *Xanthoxylum budrunga*, *Murraya koenigii*, *Origanum majorana*, *Thujopsis dolabrata*, *Mosla japonica*, and *Chamaecyparis obtusa*. In these oils we find terpinenol-4, terpinene, or both, accompanying sabinene in ten instances. One other, *Xanthoxylum rhetsa*, is reported as being more than 90 per cent sabinene. Of the seven oils in which the occurrence of sabinene is doubtful, *Melaleuca linariifolia* contains terpinenol-4 and α- and γ-terpinenes; it seems highly probable that this oil may contain sabinene. The oil of *Piper cubeba* is unique in that it is the only instance in which the isolation of 1,4-cineole has been reported; the cineole is accompanied, among others, by sabinene, terpinenol-4, and Δ^4-carene.

Considering now the occurrence of terpinenol-4, or Δ^1-menthenol-4, we find the fact definitely established in ten instances: *Piper cubeba*, *Juniperus communis*, *Cinnamomum kanahirae*, *Melaleuca alternifolia*, *Eucalyptus dives*, *Thymus zygis floribundis*, *Origanum majoram*, *Elettaria cardamomum major*, and *Chamaecyparis obtusa*. All these, except *Eucalyptus dives*, contain either sabinene or the terpinenes. In one doubtful instance, *Cupressus torulosa*, terpinene and sabinene are reported. Nine of the ten oils examined contain substances derivable from glycol III, that is, pinene, limonene, and so forth. Only one, *Eucalyptus dives*, contains compounds derivable from glycol I, the phellandrene compounds.

These facts point very strongly to the biogenetic association of sabinene with the terpinenes and terpinenol-4 on the one hand. On the other, terpinenol-4 is predominantly associated with terpinenes and sabinene.

The compounds of the glycol II group are accompanied by compounds derivable from glycol III to the exclusion of those from glycol I. Referring again to the glycol I group, we find that in one hundred and twenty-six oils the phellandrenes were accompanied ninety-seven times by substances derivable from glycol III (1,8-cineole, α-pinene, β-pinene, and limonene or dipentene), but only seven times by those from glycol II (terpinenes, terpinenols, and sabinene). The inference is plain that, since glycols I and II come from glycerol A, the further elaboration of glycerol A in the plant takes predominantly one or the other of the available routes, but not both in the same plant to any great degree. If the fact were otherwise, the derivatives of glycols I and II would be found mixed more often than in seven out of the one hundred and twenty-six instances in which it was possible under the phellandrenes, or in one out of ten possibilities in the terpinenol-4 group.

Since the 1,8-terpin series, glycol III, is derivable only from glycerol B, its members should appear in both the preceding groups (I and II). This is so in nine out of ten oils referable to glycol II, and ninety-seven out of one hundred and twenty-six phellandrene oils referable to glycol I.

The following conclusion seems warranted. In most instances, glycerol A is accompanied in the plant by glycerol B. Glycol III may be accompanied by either glycol I or II but not often by both. The practical significance of this conclusion is simply that in an oil found to contain derivatives of glycol II, finding phellandrene, piperitol, or piperitone, is unlikely, and the converse is also true. The carenes are derivable from glycols I, III, V, and VI, and may be expected in any oil. Fortunately, they are rare.

Glycol III

The derivatives of glycol III (see figure 6), from glycerol B, are the most widely distributed in nature of the terpene group. As just pointed out, they occur indiscriminately with compounds of the two preceding series, and often in predominant quantity. In short, nature shows a great preference for this group in both distribution and quantity. Now, the only difference between glycerols A and B is in the position of a hydroxyl group. In A, position 4 is occupied and in B, position 8. Whatever simpler units we may postulate as the source of these glycerols, we must explain nature's preference for a hydroxyl group in position 8.

The compounds under glycol III that are specific to this series are 1,8-cineole and β-pinene. The carenes occur also under glycols I, V, and VI, while crithmene and terpinolene occur under glycol II. The 1,8-cineole is reported definitely as occurring two hundred and sixty times, two hundred and twenty-three of which are recorded as having accompanying compounds of interest in this classification. Of these two hundred and twenty-three oils, one hundred and ninety-two contain other substances in this series, that is, α-pinene, β-pinene, terpineol, dipentene, or limonene. Sixty-three oils contain phellandrenes, piperitone, or piperitol. Seven contain terpinenol-4, terpinenes, or sabinene.

Table 2 is of interest in showing some characteristics of the distribution in eucalypts and other genera; one hundred and thirty-three oils containing 1,8-cineole are eucalypts, and one hundred and twenty-seven are not.

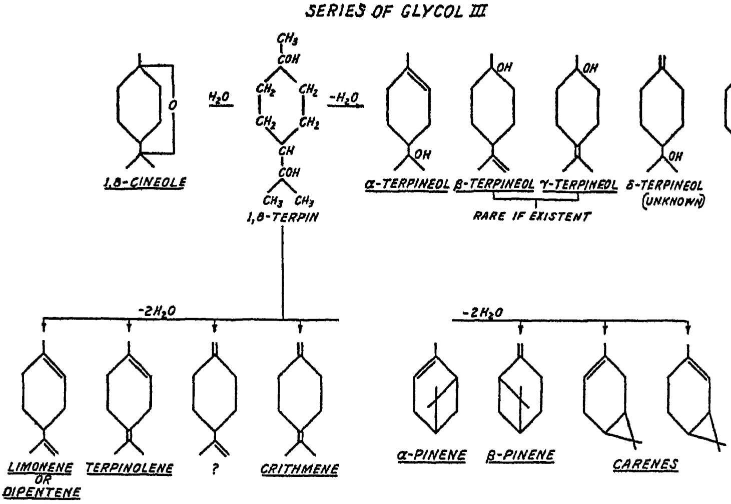

FIG. 6. THE SERIES OF COMPOUNDS POSSIBLY FORMED FROM GLYCOL III BY ELIMINATING WATER

α-Terpineol occurs in sixty-five oils. Of these oils, sixty-two contain α- or β-pinene, limonene (or dipentene), cineole, or mixtures of these substances. The phellandrene, piperitone, and piperitol compounds occur certainly in nine of these oils and are doubtfully reported in three. In all twelve instances, however, they are mixed with representatives of the glycol III series other than α-terpineol. Representatives of the series of glycol II, the terpinenol-4 series, occur in ten oils and are doubtful in one. Six of these contain substances of the glycol III series other than α-terpineol.

The association of α-terpineol with the other members of the glycol III series may be thought established.

In considering the occurrence of limonene, dipentene was called its equivalent unless the dipentene was to be taken as a pyrogenetic product. Limonene or dipentene occurs one hundred and fifty-eight times. These two compounds are associated with α-pinene, β-pinene, or both, ninety-three times; with α-terpineol twenty-four times; with 1,8-cineole thirty times; with phellandrene twenty-seven times; and with the terpinenes, including sabinene and terpinolene, eight times. Forty of these oils are not reported as containing substances considered in this classification, other than limonene or dipentene. One hundred and ten of them contain substances, the pinenes, cineole, and α-terpineol, of the series of glycol III. Hence only eight of the possibilities out of one hundred and fifty-eight are missing.

TABLE 2

The reported occurrence of 1,8-cineole

ACCOMPANYING COMPOUND	IN EUCALYPTS	IN OTHER SPECIES	TOTAL IN 223 OILS
Pinene α, β	108	63	171
Limonene or dipentene	1	29	30
α-Terpineol	5	26	31
Phellandrene β	49	16	65
Piperitone or piperitol	14	2	16
Terpinenol-4 Terpinenes Sabinene	1	6	7

The genus *Cymbopogon* is noteworthy in that eight species contain limonene, while only one, *C. caesius*, contains another member of the series, α-terpineol. Phellandrene is found in *C. martini var. Sofia*, and piperitone in *C. sennaarensis*.

The *Rutoideae* are also noteworthy. Only one species, *Ruta graveolens*, produces an oil that conforms to the series, containing limonene, pinene, cineole, and so forth. *Xanthoxylum acanthopodum* has phellandrene. The oils in the family containing limonene, six in all, consist generally of olefinic alcohols, ketones, and so forth, diosphenol, and menthone.

α-Pinene, the most widely spread of the terpenes, has been reported as occurring in three hundred and seventy-four oils at the latest count (1931). In seventy-seven of these it was not reported as accompanied by any other substances used in this classification. Thus two hundred and ninety-seven oils are available for comparative data. In two hundred and sixty-nine of these oils it is accompanied by other members of its series, glycol III. One hundred and seven of these are eucalypts in which the accompanying compound is cineole; this compound, derived from glycol III, accompanies pinene in only thirty-four of the remaining oils, one hundred and sixty-two in number. Limonene, however, is found in one hundred and four of these oils outside of the genus *Eucalyptus*, which is contrary to the statement of Singleton (11) that cineole invariably accompanies pinene. Seventeen of the one hundred and sixty-two non-eucalyptus oils contain substances of the phellandrene series from glycol I, while twenty-seven of the eucalypts contain them. As usual the eucalypts tend more strongly toward the phellandrene type of compound than does the rest of the plant world.

Pinene is accompanied fourteen times by derivatives of glycol II,—the terpinenol-4, sabinene, terpinene series.

β-Pinene, the closest relative of α-pinene, accompanies this terpene in fifty-five instances and is rarely found unassociated with it. The difficulty of isolation and identification of β-pinene when present only in small quantity renders it probable that the occurrence of this terpene is broader than is here indicated. Thirty-two of its occurrences are recorded under the *Abietineae.*

Glycol IV

Dehydration of the glycol, 2,4-menthanediol, in the usual manner gives rise to what appears to be another terpinenol-4, terpinene series (see figure 7). However, a difficulty arises from the absence of sabinene, which is predominantly associated with these compounds. Eliminating glycol IV from consideration would therefore be justified, but for one fact. Here we find thujyl alcohol for the first time; the ketone, thujone, which occurs more often, may be derived from it by oxidation. Thujene also occurs in this series, and in the first terpinenol-4 series under glycol II as well. Inspection will show, however, that thujyl alcohol and thujone are not derivable in the glycol II series without reverse hydration of thujene, which is not permitted in the present analysis. Thujene has been reported only in *Boswellia serrata,* which does not contain thujyl alcohol or thujone. Hence we are forced to assume that thujene is probably not genetically related to thujyl alcohol and thujone.

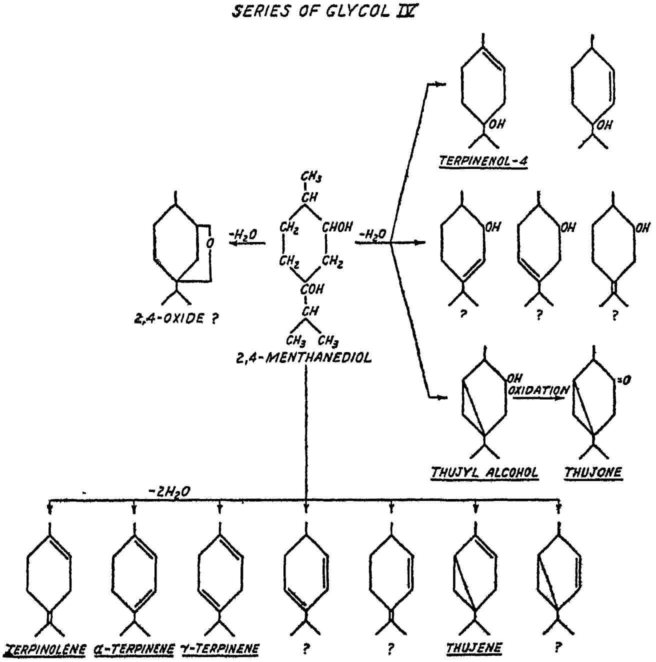

FIG. 7. THE SERIES OF COMPOUNDS POSSIBLY FORMED FROM GLYCOL IV BY ELIMINATING WATER

The ketone, thujone, is reported in fifteen oils, eleven of which contain also compounds of the glycol III series, that is, the pinene family. In none of these oils do any other members of the glycol

IV series occur. The structure of thujone accepted at present, therefore, does not fit well into the present scheme.

Glycol V

Glycol V, which gives rise only to the known compounds α-terpinene and Δ⁴-carene (see figure 8), may be dismissed for the present without further consideration.

Glycol VI

Glycol VI offers some aspects that require consideration (see figure 9). Here we find another pinene series, with 1,8-cineole and β-pinene missing. These facts would automatically exclude this glycol from consideration as existing in the *Abietineae* or the *Eucalypti*, but the occurrence of two new compounds in the series, dihydrocarveol and borneol, makes it worthy of consideration. Dihydrocarveol is reported as occurring in the oil of *Carum carvi* (caraway). It is accompanied by limonene, which is in accord with the theory presented here. Also present are carvone, carveol, and dihydrocarvone (figure 10).

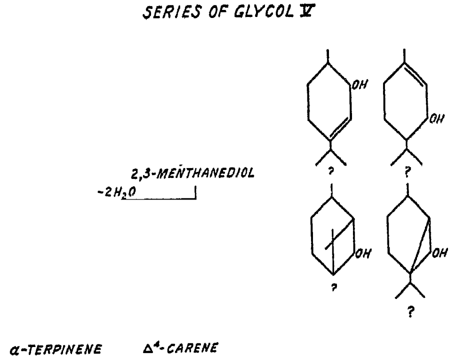

FIG. 8. THE SERIES OF COMPOUNDS POSSIBLY FORMED FROM GLYCOL V BY ELIMINATING WATER

The fitting of carvone and carveol, which are of a higher state of oxidation than the compounds under consideration, into a genetic scheme is another matter, which must be reserved for later treatment. For the time being, dihydrocarvone may be taken as related to dihydrocarveol in the way that piperitone is to piperitol.

The occurrence of borneol is confined to the series of glycol VI. It is reported authentically in one hundred and six oils, and in eighty-three instances as accompanied by compounds in this classification, distributed as follows: α-pinene, 68; β-pinene, 15; limonene or dipentene, 46; cineole, 22; phellandrenes and piperitone, 11; terpinenes, sabinene, and terpinenol-4, 3.

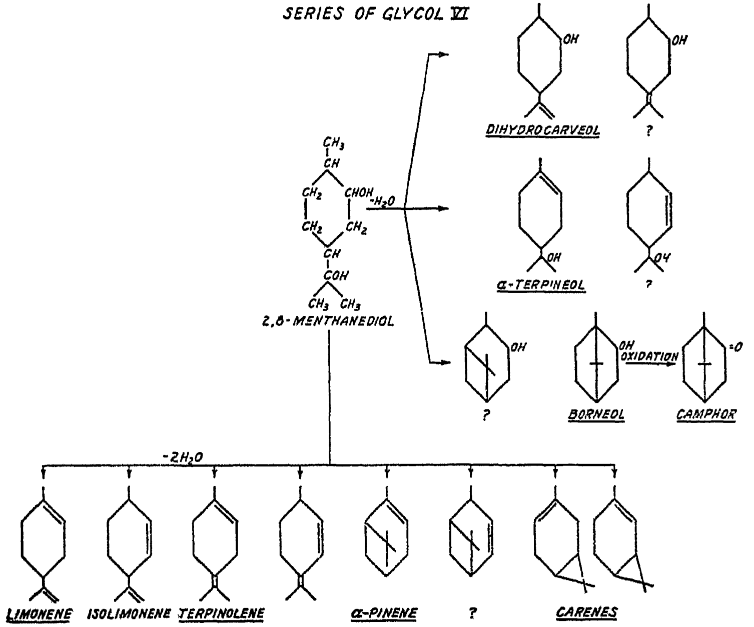

FIG. 9. THE SERIES OF COMPOUNDS POSSIBLY FORMED FROM GLYCOL VI BY ELIMINATING WATER

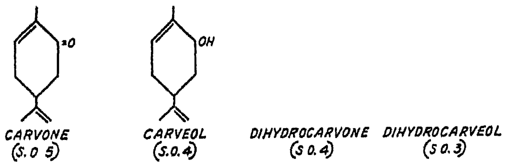

FIG. 10. CARVONE, CARVEOL AND DIHYDROCARVONE

Seventy-four oils out of the eighty-three contain α-pinene, limonene, or both, which is a sufficiently good check. With β-pinene, which occurs in the first pinene series under glycol III but not under glycol VI, its proportionate occurrence with borneol is about the same as with α-pinene. Cineole, however, shows a notable differentiation. Referable to glycol III but not to glycol VI, it occurs with α-pinene in one hundred and seventy-one out of two hundred and twenty-three possibilities, although with borneol the occurrence is only twenty-two out of sixty-eight. The cineole-rich genera, *Melaleuca* and *Eucalyptus*, together can produce only two instances of borneol, both in eucalypts from the Caucasus.

Another striking feature about borneol is its apparent association with the leaf. Of its one hundred and six reported occurrences, sixty are in leaf and twig oils and twenty-two more are in oils from herbs in which the whole plant is distilled. Thus eighty-two oils may be considered as derived wholly or in part from leaves. Further, there are five root oils. Only six oils from oleoresins contain borneol; the remainder are largely cone or fruit oils, with one from a bark and one from a wood.

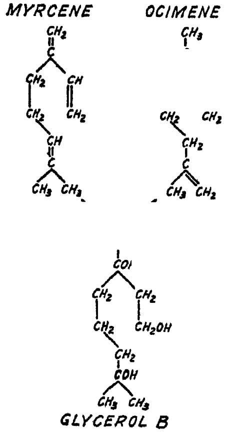

FIG. 11. THE DERIVATION OF THE OLEFIN TERPENES

The low association of cineole with borneol, contrasted with its high association with pinene, which occurs in both series, may be confirmatory evidence of the biogenetic disassociation of borneol and cineole. The derivatives of glycol VI have been found most abundantly in plant structures of leaf or fruit type, and are frequently accompanied widely by derivatives of glycol III.

The occurrence of α-pinene and limonene in both these apparently important series must have a great deal to do with the wide occurrence of these compounds.

The possible derivation of the olefinic terpenes, myrcene and ocimene, from glycerol B is given in figure 11. Clearly, myrcene can be derived from either the 1,3,4- or the 1,3,8-glycerol, although ocimene can be derived only from the latter. Also, both geraniol and linaloöl can be derived from glycerols A and B, but only geraniol from C and D.

CONCLUSIONS

The predominant family of terpenes and near relatives in the plant world is the pinene group.

Family I: α-Pinene
β-Pinene
Limonene
Dipentene
Carenes
Terpinolene (not specific)
Crithmene
1,8-Cineole
α-Terpineol
Borneol (camphor)
Dihydrocarveol

According to association and derivation from glycols III and VI, which are the only glycols with hydroxyl on carbon atom 8, this family should be subdivided as follows:

Subfamily IA: α-Pinene
β-Pinene
Limonene
Dipentene
Carenes
Terpinolene
Crithmene
1,8-Cineole
α-Terpineol

Subfamily IB: α-Pinene
Limonene
Dipentene
Carenes
Terpinolene
α-Terpineol
Borneol (camphor)
Dihydrocarveol

Second in importance as to occurrence is the phellandrene group, derivable from glycol I.

Family II: α-Phellandrene
β-Phellandrene
Carenes
Terpinenes
Piperitol (piperitone)

Family II is more often associated with subfamily IA than with any other group.

Less prevalent than the others, but associated mostly with family I, is family III.

Family III:	Terpinenes	1,4-Cineole
	Sabinene	Terpinenol-4
	Thujene	Thujyl alcohol (thujone)[2]
	Terpinolene	
	Crithmene	

According to association and derivation from glycols II and IV, which are marked by possessing hydroxyl on carbon atom 4, this family should be subdivided as follows:

Subfamily IIIA:	Terpinenes	1,4-Cineole
	Sabinene	Terpinenol-4
	Thujene	
	Terpinolene	
	Crithmene	
Subfamily IIIB:	Terpinenes	Terpinenol-4
	Thujene	Thujyl alcohol (thujone)

If the biogenesis of these substances occurs along the lines indicated, which hypothesis is supported by the evidence accumulated, it is clear that small changes in intercellular mechanism may shift the composition of the resultant oil considerably, but the classification of the oil according to the above scheme should remain the same. This classification should be of some value in working out differences in closely related species.

The mechanism of the formation of the hypothetical glycerols can not yet be logically explained on the basis of our present knowledge. Further research on the water-soluble components of plants yielding volatile oils may yield substantiating evidence for the above hypothesis. For the present, the classification given has only the support of the evidence of biological association submitted. This, however, has the definite merit of following actual occurrence rather than an artificial structural classification, and should prove to be of value in isolation studies as well as furnish a unified basis for the study of terpene chemistry.

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[2] Structure and occurrence do not conform.

Perhaps future work will isolate certain of the compounds now indicated as undiscovered, as well as others whose formulas have been omitted. Should they be associated as indicated here, considerably more weight will be added to this classification.

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PROBLEMS OF MODERN ENZYME CHEMISTRY[1]

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Munich, Germany

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At this time a new approach to the investigation of physiologically active substances seems to be warranted. This group of substances, which comprises hormones and enzymes, but which also includes—in certain respects—the proteins, should not be treated in a purely "static" (descriptive) manner; a more dynamic consideration promises further insight into their constitutional peculiarities. Changes in the mineral constitutents of the crust of the earth, accomplished by processes of solution through geologic periods, find an analogy within mere seconds or fractions thereof in the autolysis of living, dying, and killed cells.

Certain substances in glands or leucocytes display little resemblance to those chemicals of guaranteed constancy of composition and properties which one finds listed in chemical catalogues. Little attention has been paid to the fact that the processes of solution and extraction, preliminary to the study of physiologically active substances, are entirely different from the simple phenomenon of dissolving stable organic compounds. We deal with very reactive substances which must be extracted from the ever-changing array of allied substances, likewise endowed with high reactivity. There always lurks the danger—which indeed often materializes—that denatured or changed derivatives are isolated instead of the original natural compounds.

Enzymes are more suitable for these dynamic tests than hormones, although the latter offer the additional attraction of practical medicinal importance. The biologists measure hormonal activity by ingenious and delicate methods such as the cockscomb test for the male sex hormone devised by my famous Chicago colleagues. The quantitative estimations of enzymes by measurement of reaction velocities have the advantage of speed and accuracy. We control each step in the preparative purification of enzymes by quantitative analysis. They sometimes—indeed frequently—yield incorrect values in the case of enzymes, as their action is influenced by activators and inhibitors. Nevertheless, these measurements are always necessary, and discordant results in this field may become the starting points for remarkable discoveries.

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[1] The Willard Gibbs Medal Address for 1933, delivered at the Joint Session of the Biochemical, Medical, and Organic Divisions of the American Chemical Society at the Eighty-sixth Meeting, in Chicago, September 14, 1933.

The chemical changes during autolytic processes concern not only the substrates, but the enzymes themselves, and influence their essential characteristics. I wish to report today several observations on this phenomenon in the case of leucocyte amylase. Sometimes chemical changes involve those complexes which account for the protoplasmic linkage and which determine its solubility. Sometimes they have to do with the protective mechanism that prevents the enzyme from diffusion. Generally, enzyme research has been concerned with the study of soluble enzymes, or more properly, with the soluble portion of enzymes. It appears, however, that the fraction of an enzyme which cannot be attacked by simple processes of solution, and which can be demonstrated to be present in organ, tissue, and cell residues, is definitely characterized. Those enzymes which are chemically bound to the protoplasm and which are insoluble because of the chemical constitution of those complexes, we term "desmo"-enzymes. They stand in contrast to the well-known "lyo"-enzymes which in their natural state are soluble in water and glycerol, the latter property being advantageous for the avoidance of autolysis.

We unwittingly entered this realm of desmoenzymes twenty-seven years ago, when comparing the chlorophyll of a variety of plants. Before solving the difficult task of isolating chlorophyll in substance, we noted three points essential for the recognition of chlorophyll, and for the comparison of the innumerable instances of its occurrence: (1) Its content of magnesium, 4.5 per cent coördinately bound magnesia; highly unstable green carboxylic acids are obtained by the saponification of dissolved chlorophyll, the so-called chlorophyllins, which still contain magnesium and are suitable for its determination. (2) Its content of phytol, the alcohol of formula $C_{20}H_{39}OH$. (3) The main portion of the big molecule, the porphin nucleus of the pigment, that is, of the two chlorophylls *a* and *b*, is characterized by two carboxylic acids of the pyrrole series, the olive green phytochlorin *e* and the red phytohodin *g*. These are formed by subsequent hydrolysis with acids and alkali. Under certain very mild conditions, these two carboxylic acids are the only products; under less favorable conditions mixtures of numerous split-products are generated.

The mild treatment of chlorophyll with acid results in the formation of a difficultly soluble olive-colored wax, phaeophytin, in which the ester group is intact. It contains 33 per cent of the alcohol phytol. It is the magnesium complex which is obviously destroyed by this acid treatment, while left intact by treatment with alkali, just contrary to the case of the phytol ester linkage. Chlorophyll from more than two hundred plants of different classes and geographic origin showed complete uniformity. However, this result was only obtained by way of a peculiar detour; originally great variations in the phytol percentages were found with different plants, for instance, instead of 33 per cent only 17, or 6, or 2, or 1 per cent. The plants with chlorophyll of apparently low phytol content served as material for a startling discovery. They furnished "crystallized" chlorophyll, a compound of marvelous beauty, difficultly soluble dark green crystals with 6 per cent magnesia. Russian botanists had discovered them in microscopic sections. When we chemists penetrated to this point, the nature of crystallized chlorophyll was still veiled in darkness. Was it a natural product or an artificial one? This puzzle was solved by examination of the process of solution. When chlorophyll is rapidly withdrawn from the leaves and the solution at once separated from the leaf residue, then the phytol content is always normal, one-third. But if the alcoholic solution of the pigment remains in prolonged contact with the leaves, the phytol percentage drops more or less, with some plants nearly to zero. In such cases, phytol-free insoluble crystallized chlorophyll is formed instead of the waxy phytol-containing variety. The phytyl group has been replaced by ethyl, on one single carboxyl group of the chlorophyll. This reaction, an alcoholysis, is brought about by the enzyme chlorophyllase, which accompanies chlorophyll in leaves in variable quantities. Chlorophyllase in aqueous medium causes hydrolysis to free carboxylic acids, the chlorophyllides; even the partial synthesis of chlorophyll from these acids plus phytol was accomplished by means of this enzyme. Chlorophyllase, according to our present terminology, is a desmoenzyme; it remains in the leaf residue after treatment with all solvents. Have these leaf residues, the chaff so to speak, well-defined enzymatic character? They certainly have; they react only with the ester chlorophyll, and a more recent investigation showed that the desmoenzyme is inactive after thorough washing. Addition of calcium ion restores its activity, a distinctive characteristic.

Changes like that suffered by chlorophyll through the action of solvents on the leaf substance, also threaten other plant constituents during extraction, especially alkaloids with ester groups and glucosides. This principle guided my former pupil, A. Stoll, who was my assistant during the study of chlorophyllase and who is now director of a chemical factory in Switzerland. In an excellent research on digitalis glucosides, he succeeded in isolating three new glucosides—digilanid A, B, and C—by the most delicate exclusion of enzymatic hydrolysis during extraction from *digitalis lanata.* They are tetraglucosides and contain three molecules each of digitoxose and one molecule of glucose, besides an acetyl group. They are the hitherto unknown parent substances of all the various digitalis glucosides, digitoxin, gitoxin, gitalin, and the corresponding aglucones digitoxigenin, gitoxigenin, and digoxigenin. The original glucosides are accompanied by specific glucosidases causing partial cleavage of the sugar. The known digitalis substances are secondary products; the new ones are the natural parent substances.

The observation of the insolubility of chlorophyllase induced Waldschmidt-Leitz and myself to attempt the purification of castor-bean lipase as an example of an insoluble enzyme. This desmoenzyme is very unstable towards water or glycerol unless it is protected by oil. It is especially labile in dried and defatted condition. This lipase can be obtained in higher concentration by shaking its emulsions in oil with aqueous reagents, e.g., dilute alkali, which removes proteins.

Other methods for the systematic increase of enzyme concentration apply to soluble enzymes, especially the methods of specific adsorption, developed for this purpose. The investigation of various lyo- and desmo-enzymes led to the first, although primitive, conception of the structure of enzymes. We visualized this structure as a specific active group with a high-molecular colloidal carrier. We shall examine today whether this conception proved fruitful and whether it is already possible to make any statements as to the properties of the specific groups and molecules on the one hand and the importance and influence of the colloidal carrier on the other hand.

Strong hydrochloric acid, or even better, pepsin in acid medium causes a remarkable change in the nature of castor-bean lipase. After such treatment, it coincides in its properties with the lipase of the germinating seed. The lipase of the (dormant) bean, spermato-lipase, and the lipase of the germinating seed, blasto-lipase, behave like two entirely different enzymes. The one acts in acid medium, the other at neutrality. The second one is far superior for synthetic reactions. The characteristic transformation of castor-bean lipase must be interpreted as partial proteolysis of the colloidal carrier.

A few fundamental facts have been ascertained regarding the specific active groups of enzymes. The way had been paved primarily by the high degree of enzyme concentration achieved through extensive purification; but accurate observations and improvements in the (preliminary) procedures, leading to solution, contributed a great deal to these results. A good illustration for this methodical development is furnished by the case of yeast saccharase. Previously solution of this enzyme was effected, for instance, by quantitative autolysis of yeast, whereupon the concentration of the dissolved enzyme should correspond with that in the yeast cell. Or, yeast was treated with water in the presence of a preservative, under the assumption that the enzyme could diffuse from within the cell. Only a minute percentage, and an unknown one besides, passed into solution, and even that without significant increase of purity. In reality, saccharase cannot be withdrawn from an intact cell, but poisoning of the yeast cell is the sine qua non for solution of the enzyme. Once autolysis, a multitude of enzymatic hydrolyses, is initiated, then there is one definite singular reaction, the liberation of the enzyme saccharase, which can be favored selectively among the other autolytic processes. Thus, one can accomplish complete liberation of the saccharase, together with as little as one-twentieth of the inert contents of the yeast cell. An investigation carried out by Dr. C. D. Lowry in my laboratory afforded additional aid. By a special fermentation process, yeast could be enriched in saccharase fifteen to twenty times. A combination of these experiences yielded enzyme solutions which, to begin with, were three hundred times superior in purity to ordinary yeast. Systematic development of adsorption methods permitted further considerable increases of enzymatic purity in the case of saccharase as well as in that of peroxidase or pancreas amylase.

The method of selective adsorption by specific adsorbing agents was also fruitfully developed in another direction, namely, for the separation of enzymes from each other. The first example was the group of pancreatic enzymes, amylase, lipase, and trypsin. Another step in the progress was the separation of such closely related enzymes as saccharase and maltase. The last application of greater importance was the resolution of animal and vegetable proteases into their numerous components by Waldschmidt-Leitz and by Grassmann, and the segregation of β-glucopolysaccharidase, specific for cellulose and cellodextrins, from β-glucoöligosaccharidase, capable of hydrolyzing the lower molecular carbohydrates originating from cellulose. This separation by means of aluminum metahydroxide has been published this summer by Grassmann and Zechmeister.

Since saccharase becomes soluble only through a definite enzymatic process, one might assume that it is tied to the protoplasm. This view seemed to be supported by the following experiment. Autolytic reactions, essential for the solution of saccharase, can be eliminated by treatment with warm ethyl acetate, which destroyes the enzyme responsible for the liberation of saccharase. Then the yeast cell may be emptied by the action of pepsin or trypsin with complete recovery of the saccharase originally present. Yet this saccharase remains in the cell residues, from which afterwards it may be dissolved by the action of plant amylase or plant proteinases. Was the enzyme linked to the protoplasm? The answer is no, it was only protected and fixed; so to speak tucked away by the cell membrane which, according to the two possibilities of attack, must consist of protein linked to carbohydrates. For, according to more recent experiments, yeast may be finely triturated with liquid air and treated with anhydrous glycerol, strictly eliminating all autolytic processes. Then saccharase passes into solution, after complete, but purely mechanical, destruction of the cell membrane. We propose to call an enzyme of this type, protected from solution by mechanical, not by chemical means, an "endoenzyme."

This protection of endoenzymes against diffusion is in accord with the properties and the behavior of the yeast cell. A comparison with other cells and with glandular tissues reveals gradations of solubility and stability of what might be called anchorage; little attention has been paid to these facts up to the present time, and it has been customary to prepare enzyme solutions with aqueous media or glycerol, without any regard to the possibility of autolytic reactions, while the share of enzyme remaining in tissue, gland, and organ residues was neglected. However, if the much investigated, long known enzyme pepsin was advantageously prepared by five days' digestion with an excess of 0.5 per cent hydrochloric acid at 37°C. according to C. A. Pekelharing, this is certainly not the dissolving of a soluble enzyme, but, for the most part, the liberation of an insoluble, plasma-linked pepsin. If we avoid autoproteolysis by treatment of stomach mucosa with dilute hydrochloric acid at 0°C., desmopepsin is left in the tissue residue and can only be rendered soluble by various proteolytic procedures.

Analogously, a great portion of trypsin is found ready for secretion as a lyoenzyme in the pancreas gland; but another part is bound as desmotrypsin in the inactive state and forms an insoluble complex together with a precursor of enterokinase, its natural activator. These conditions are highly significant for the decision of the question whether certain enzymes are simply identical with certain proteins.

Histozyme, a kidney enzyme, which decomposes hippuric acid and conjugated bile acids, occurs to a greater extent as lyo- or as desmo-enzyme according to animal species. In dog kidney it is easily soluble, in horse kidney insoluble; hog kidney contains partially soluble, partially insoluble, histozyme.

Deeper insight is offered by the study of the white blood corpuscles, which have no secretory function. They are extremely prone to autolysis, but if this is avoided by momentary desiccation, then leucocytes contain, for instance, trypsin almost completely plasma-bound, as proven by careful treatment with anhydrous glycerol.

The desmoenzymes investigated are not uniform as a rule. For example, desmoamylase of leucocytes consists of one fraction, which is soluble in alkali phosphate and other fairly neutral electrolytes. From the cell residues, a second fraction can only be rendered soluble by proteolysis, e.g., by papain. A third fraction, absolutely resistant against proteinase, is left over. The comparison of these fractions with each other and with the lyoenzyme shows that the colloidal carrier proper of the enzyme, the indispensable component of its molecule, may in turn be associated with other high-molecular substances, which determine its solubility and resistance against attempts at isolation. The enzyme may occur in the form of solid solutions or adsorption compounds with proteins; its colloidal carrier may also be chemically combined with proteins and other substances of high molecular weight.

The significance of the protein content of enzymes has become the subject of a fruitful discussion between some American colleagues and ourselves. While our own efforts in the case of saccharase, amylase, and other enzymes aimed at the gradual and, if possible, complete liberation of enzymes from protein, these American colleagues proceeded exactly in the opposite direction. They succeeded in the isolation of proteins endowed with enzymatic activity. The isolation of urease by Sumner, of pepsin by Northrop, and of trypsin by Northrop and Kunitz in the form of crystallized proteins are brilliant discoveries and important preparative successes. But it remained doubtful whether the protein content of these enzymes really forms an indispensable constituent and whether indeed "the proteolytic activity is a property of the protein molecule itself." Dyckerhoff and Tewes in Munich and Waldschmidt-Leitz and Kofranyi in Prague were able to replace the protein, which carried pepsin activity, by vegetable protein. According to these authors, the enzyme of a pepsin solution can be completely adsorbed on certain seed globulins, while the original protein component remains completely in the mother liquor without peptic activity. Thus the crystallized protein should not be considered identical with the enzyme; it cannot even be acknowledged as its indispensable colloidal carrier.

The existence and significance of the true colloidal and molecular carrier of the active group can be proven, however, by delicate procedures, which cause well-defined changes in the properties of an enzyme, similar to those mentioned in the case of castor-bean lipase and to those encountered with the peroxidase action of oxyhemoglobins. Unpublished work on leucocyte amylase which Miss Rhodewald has carried out with me, exemplifies this possibility. It does not deal with the differentiation of the various fractions of desmoamylase, mentioned before, but with transformations of lyo- (and desmo-) amylase, changes of sharply defined properties without loss of enzymatic activity. Such characteristic properties are as follows: (a) Amylase may, or may not, be inhibited by glycerol. (b) It may be independent of the presence of phosphate, that is, completely active with or without phosphate ion, or it may be inactive without the addition of phosphate.

These two characteristics permit the existence of four amylases, with the properties a+ b+, a− b+, a+ b−, and a− b−. We have learned to prepare these four amylases, one only as a by-product, from leucocytes, or rather to prepare four lyoamylases and the four corresponding desmoamylases or indeed groups of desmoamylases. They all belong, according to E. Ohlsson's classification of dextrinogenic and saccharogenic amylases, to the former group and to the alpha-amylases of R. Kuhn.

One should not object to the complicated nature of these results. The observations are accurate, and cannot be thrust aside. There are further instances where analogous observations will serve the characterization of enzymes and the study of their primary changes.

A few examples will be given here for the individual leucocyte amylases. Fresh leucocytes yield amylase solutions with glycerol which are inactive without phosphate, not inhibited by glycerol, and very unstable in aqueous solution. This amylase is generated during the rapid killing of the leucocytes in glycerol from another amylase of opposite properties (−a, −b from +a +b). Leucocytes suddenly dehydrated by an excess of acetone contain the primary amylase, which requires no phosphate for activation. Hence, with glycerol a solution may be prepared without any manifest amylase action, but which nevertheless contains amylase, inhibited by glycerol, and independent of phosphate. Its presence can be proven by dialysis of the glycerol, and it is active with or without phosphate. The dialyzed solution, however, does not contain the original, but a changed amylase. Its property of being inhibited by glycerol has disappeared; addition of glycerol is now without effect: −a +b. In some instances a great difference of effect was observed with and without phosphate owing to the presence of a fourth lyoamylase +a −b. The transitions of these amylases into one another are so easily accomplished that the physiological difference between batches of leucocytes seems sufficient to yield amylase −a +b and sometimes even −a −b instead of the primary +a +b.

The residues of rapidly dried leucocytes, after treatment with glycerol, contain the desmoamylase +a +b, independent of phosphate and inhibited by glycerol. It is more stable towards water than the corresponding lyoenzyme. Leucocytes treated in fresh moist condition with glycerol contain desmoamylase, not inhibited by glycerol and only active in presence of phosphate (−a −b). It is labile and loses its activity within a few hours in aqueous solution. The characteristic properties mentioned will suffice to analyze mixtures quantitatively.

The described changes seem to occur on two functional groups, not identical with, but of decisive influence on the specific active group of the enzyme.

It takes place presumably on the molecular carrier, whether the latter is still anchored in the protoplasm (desmo) or dissolved (lyo). While these experiments are merely a first attempt at subjecting the entire enzyme molecule to chemical interpretation, there are a few cases where the specific active group, postulated by our theory, has been chemically defined. Respiration ferments have been recognized by O. Warburg and by D. Keilin as iron porphyrin complexes with unknown colloidal carriers. Furthermore, Zeile and Hellström succeeded in the case of catalase, and Kuhn, Hand, and Florkin in that of peroxidase, after far-reaching purification by adsorption methods, to adduce evidence that these enzymes owe their activity to iron porphyrin complexes.

However, not only the highly active protein crystals of our American colleagues, but even purified catalase and peroxidase are far from the point where one might consider them as pure preparations. Peroxidase, as characterized spectroscopically by Kuhn, is still diluted by a thousandfold excess of foreign material according to its content of active iron. Thus the computable reactivity of an enzyme molecule reaches a value near the theoretically possible limit, namely, occurrence of reaction at every collision of enzyme and substrate molecule. This computation is of course based on the presumption that each effective collision generates a stoichiometric amount of reaction product.

Is this assumption cogent? Newer theories of chain reactions in the auto-oxidation of inorganic substances are based on the remarkable observations of H. L. J. Bäckström and have been developed by J. Franck and F. Heber. This principle is suitable, as my friend Haber and I have stated, for the explanation of numerous organic and biological processes, such as oxidations, dehydrogenations, and dismutations. We assume the formation of monovalent radicals, whose function is the generation of polymolecular reaction chains. Accordingly, reactions like the cleavage of hydrogen atoms do not proceed in pairs, but the first step consists in the cleavage of a single hydrogen atom. A first radical is formed, for instance, CH_3CHOH—. This radical, together with oxygen, generates a second radical —OH, and this in turn with alcohol the first radical and so on.

By this short reference to reaction chains and chain reactions, as applied to enzymes, we have abandoned the solid ground of facts and have embarked on the rocking ship of hypothesis.

Whether we deal with such tentative explanations, or with the controversial protein nature of enzymes, I feel that it is not important for the scientist whether his own theory proves the right one in the end. Our experiments are not carried out to decide whether we are right, not to prove that we are right, but to gain new knowledge. It is for knowledge's sake that we plow and sow. It is not inglorious at all to have erred in theories and hypotheses. Our hypotheses are intended for the present rather than for the future. They are indispensable for us in the explanation of the secured facts, to enliven and to mobilize them and above all, to blaze a trail into unknown regions towards new discoveries.

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